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Universal biological scaling and mortality

(basal metabolism/life-span/molecular damage)

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ABSTRACT **Universal scaling relations for basal metabolism, heart rate, and life-span are presented in a physically transparent form with no adjustable parameters. Their accuracy is a few percent for animals ranging from invertebrates to mammals. They suggest that natural death is related to irreparable molecular damage to specific cells or molecules.**

Section 1. Scaling in Biology

Universal quantitatively accurate laws for few variables are a characteristic feature of physics. In biology the number of parameters that comprehensively describe a living being is unspecified. Moreover, many of them (e.g., the heart rate), even within a given species, vary with age, size, sex, state (sleep, rest, exercise, fast), etc. Although from bacteria to a blue whale the mass changes by a factor of 10^{20}, biology yields some very general and rather accurate relations. Rubner in 1883 and then in 1908 presented two of the first scaling relations in biology: basal (i.e., resting) metabolism is proportional to the body surface (1); and the total energy expenditure per life-span for five species of domestic animals is approximately constant (2) at about 200 kcal (1 kcal = 4.18 kJ)/g of body weight. Extensive studies (3–9) led to various empirical allometric relations with two or three adjustable parameters each. The most accurate results are obtained for placental mammals (4, 10). Their basal oxygen consumption rate $\dot{V}_O$ (in ml/sec), life-span t_l (in sec), and heart rate ω_h (in sec^{-1}) are related to their mass M (in kg) by the allometric equations (4)

$$\dot{V}_O = 0.2\ M^{0.76};\quad t_l = 4 \times 10^8\ M^{0.2};\quad \omega_h = 4M^{-0.25}. \qquad [1.1]$$

The factors in Eq. **1.1** depend on the units of $\dot{V}_O$, t_l, and ω_h. (For instance, if M is in g, then the factors change correspondingly to 10^{-3}, 10^8, and 0.7.) They have a fractal dimensionality (e.g., 0.2 ml × sec^{-1} × $kg^{-0.76}$) and no explicit physical or biological meaning. For different classes the factors and exponents are different.

In this paper I present universal scaling relations for basal metabolism, heart rate, and life-span in a physically transparent form (*Section 2*) and verify (*Section 3*) their accuracy within a few percent for animals ranging from invertebrates to mammals (Fig. 1) and within 10% for protozoa and bacteria with oxygen metabolism. The relations imply that the energy consumption per body atom per biologically characteristic time (e.g., a heartbeat in animals with a heart) is the same within an order of magnitude in all animals (universality) and in all basic processes (superuniversality). Superuniversality may be seen as a biological "within an order of magnitude" counterpart of the well-known (11) physical energy equidistribution (between degrees of freedom). The relations also suggest the origin of natural death (irreparable molecular damage to vital cells), its physical mechanism, and the existence of specific "death cells/molecules," whose damage is lethal (*Section 4*). The deviations of a few percent from universality may provide an accurate quantitative measure of the biological difference between different classes of animals.

Conversely, if one postulates the molecular origin of death and superuniversality, one obtains universal relations with no adjustable parameters.

Outstanding problems are discussed in the last section. I conclude with a summary.

Section 2. Universal Scaling

Let us start with presenting Eq. **1.1** in a physically and biologically suggestive form.

An animal body consists mostly of water. Its volume is $\sim V = M/\rho_w$ ($\rho_w = 10^{-3}$ kg/ml is the density of water), and it contains $\sim N = 3M/M_w$ atoms (3 per water molecule with mass $M_w \sim 3 \times 10^{-26}$ kg). (Here and below $\sim$ denotes an equality within an order of magnitude.) Multiply the last equation in **1.1** by $V^{1/3} = 10M^{1/3}$ (where $V^{1/3}$ is in cm and M is in kg). Then

$$\omega_h V^{1/3} = uM^{0.08},$$

$$u = 40\ \text{cm/sec},\quad V = M/\rho_w. \qquad [2.1]$$

Substitute u from Eq. **2.1** into Eq. **1.1** and calculate the life-span basal oxygen molecule consumption $N_l = N_O\dot{V}_O t_l$ (N_O, $\simeq 3 \times 10^9$ ml^{-1}, is the oxygen molecule density); the basal energy consumption $E_h = \varepsilon_1\dot{V}_O/\omega_h$ per heartbeat [ε_1 = 4.8 cal/ml $\simeq 2 \times 10^5$ kg × cm^2/sec^2 is the oxidation energy (10)] and $E_O = \varepsilon_1\dot{V}_O t_O$ per the time $t_O = V^{1/3}/u$. Relate the energies E_h and E_O to the microscopic energy $M_w u^2$. [Later I prove it is $\sim$ the kinetic energy of the blood flow per blood (mostly water) molecule.] The result may be presented in the following form:

$$0.1N_O\dot{V}_O t_l = A_1 N;\quad N = 3M/M_w; \qquad [2.2]$$

$$\varepsilon_1\dot{V}_O/\omega_h = A_2 N M_w u^2; \qquad [2.3]$$

$$\varepsilon_1\dot{V}_O V^{1/3}/u = A_3 N M_w u^2;\quad V = M/\rho_w. \qquad [2.4]$$

According to these equations, $A_1 = 0.1N_O\dot{V}_O t_l/N$; $A_2 = \varepsilon_1\dot{V}_O/\omega_h N M_w u^2$; $A_3 = \varepsilon_1\dot{V}_O V^{1/3}/N M_w u^3$. Substitute into these relations $N = 3M/M_w$ from Eq. **2.2**; $\dot{V}_O$, t_l, and ω_h from Eq. **1.1**; $u = 40$ cm/sec and $V = M/\rho_w$ from Eq. **2.1**; and $N_O \simeq 3 \times 10^{19}$ ml^{-1}, $M_w \simeq 3 \times 10^{-26}$ kg, $\rho_w = 10^{-3}$ kg/ml, and $\varepsilon_1 \simeq 2 \times 10^5$ kg × cm^2/sec^2. Obtain $A_1 \simeq 2M^{-0.04}$; $A_2 \simeq 2M^{0.01}$; and $A_3 \simeq 2M^{0.09}$.

For mammals M changes from 0.003 kg for a masked shrew (*Sorex cinereus*) to 4000 kg for an elephant (*Elephas maximus*). So, $M^{0.04}$ changes by 30%, $M^{0.01}$ by 1%, and $M^{0.09}$ between 0.7 and 2. Thus, $A_3 \sim A_1 \simeq A_2 \simeq 2$. Eqs. **2.2–2.4** have

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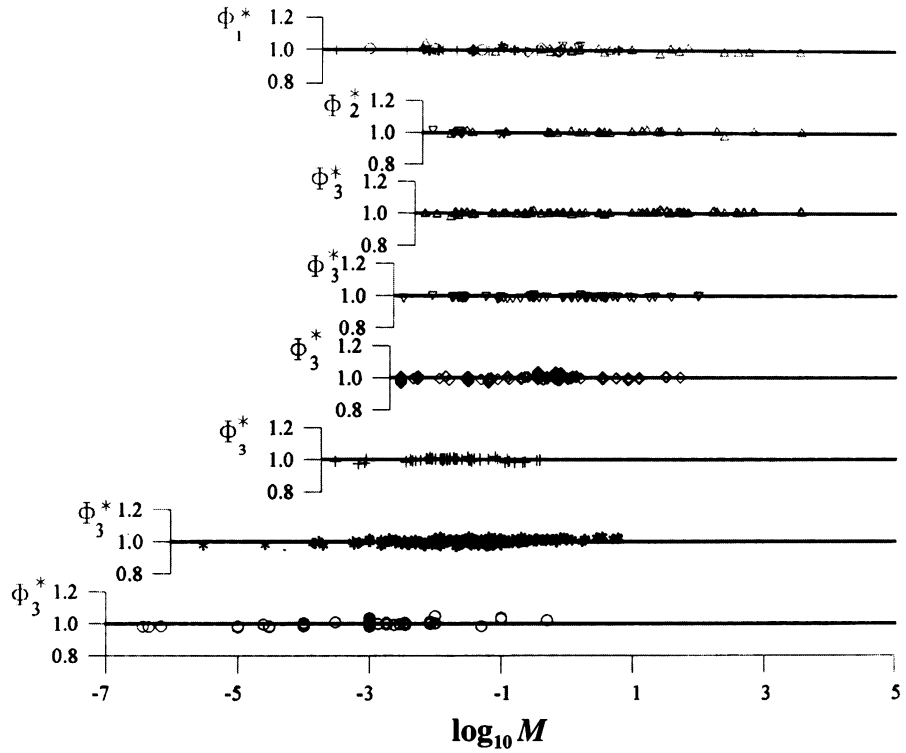

FIG. 1. Theoretical (solid lines) and experimental reduced basal oxygen consumption vs. $\log_{10}M$ (animal weight M is in kg) for mammals (△), birds (▽), reptiles (◇), amphibians (+), fishes (*), and invertebrates (○). Vertical scales are offset for clarity.

the following features—cf. Eq. **1.1**. (*i*) The factors A_i are dimensionless numbers ~ 1. (*ii*) Apart from numerical factors $A_i \sim 1$, they contain only a single universal velocity $u = 40$ cm/sec, which is ~ the mean blood velocity (20–40 cm/sec by refs. 4 and 12). (*iii*) They are physically transparent. Eq. **2.2** implies that the total number $N_l = N_O\dot{V}_O t_l$ of oxygen molecules consumed per life-span is $10A_1N \sim 20N$, where N is ~ the total number of atoms in a body. Thus, ~20 oxygen molecules are consumed per body atom per life-span. (This is consistent with Rubner's 200 kcal/g per life-span.) By Eqs. **2.3** and **2.4**, the basal energy per body atom per heartbeat ω_h^{-1} is $E_h/\omega_h N = \varepsilon_1\dot{V}_O/\omega_h N = A_2M_wu^2 \sim 2M_wu^2$ and per blood circulation time $\sim t_O = V^{1/3}/u$ ($V^{1/3}$ is ~ a body size) is $E_Ot_O/N = \varepsilon_1\dot{V}_OV^{1/3}/uN = A_3M_wu^2 \sim 2M_wu^2$. Since u is ~ the blood flow velocity, M_wu^2 is ~ the blood flow energy per molecule. I conjecture that these features are universal and that Eqs. **2.2–2.4** are valid for all animals from invertebrates to mammals. (Later I discuss their applicability to protozoa and bacteria.) For these animals the total number of body atoms changes by 10 orders of magnitude, from $\sim 3 \times 10^{19}$ for a crab, *Uca pugilator megalops*, to $\sim 4 \times 10^{29}$ for an elephant, *Elephas maximus*. So it is convenient to employ a logarithmic scale and to introduce

$$\Phi_1 = [\ln(0.1N_O\dot{V}_Ot_l)]/\ln N;$$

$$\Phi_2 = [\ln(\varepsilon_1\dot{V}_O\omega_h^{-1}/M_wu^2)]/\ln N;$$

$$\Phi_3 = [\ln(\varepsilon_1\dot{V}_OV^{1/3}/M_wu^3)]/\ln N. \qquad [2.5]$$

By Eqs. **2.2–2.4**,

$$\Phi_i \equiv 1 + \phi_i; \quad \phi_i = (\ln A_i)/\ln N; \quad i = 1, 2, 3. \qquad [2.6]$$

For all animals $\ln N \sim 50$. So, if my conjecture of $A_i \sim 1$ for all animals is valid, then within the accuracy $\phi_i \sim 0.02$ one arrives at the universal relations with no adjustable parameters:

$$\Phi_i = 1. \qquad [2.7]$$

The root mean squared fluctuation $\delta_i = [\overline{(\phi_i - \overline{\phi_i})^2}]^{1/2}$ yields the accuracy of this scaling. The value of $(\phi_i - \overline{\phi_i})$ is a quantitative characteristic of a given species. (A bar denotes an average with respect to the considered species.)

The basal oxygen consumption is related to a set of chemical reactions (e.g., hemoglobin oxygen binding), whose rate and outcome depend (11) on temperature T exponentially. In a narrow (compared to a thermodynamic temperature ≃ 300 K) temperature interval this implies

$$\dot{V}_O(T) = \dot{V}_O(T_O)\exp(\alpha\Delta T), \quad \Delta T = T - T_O, \qquad [2.8]$$

where T_O is a fixed temperature and T is the body temperature for mammals and birds and the ambient temperature for others. Eq. **1.1**, and thus Eqs. **2.2–2.4**, corresponds (4, 10) to $T_O = 37°C$. For mammals (4, 10) $\alpha \simeq 0.07$ degree^{-1}. For other classes it is slightly different (4), but the impact of the change is always relatively small. So, below I use $\alpha = 0.07$ as the universal value.

In the next section I verify the universality of $\Phi_i = 1$.

Section 3. Verification and Superuniversality

The calculation of Φ_i, by Eq. **2.5**, reduces to experimental data. The plots of $\Phi_i^* \equiv \Phi_i - \overline{\phi_i}$ vs. $\log_{10}M$ (M is in kg), according to all basal data available in ref. 10, are presented in Fig. 1 for animals ranging from invertebrates to mammals. Body and ambient temperatures are accounted for by Eq. **2.8**.

The data are most comprehensive for mammals and birds. For other classes of animals they are rather inaccurate. For instance, "the rates ($\dot{V}_O$) obtained for fish are 2–3 times the resting rate . . . for reptiles the rates show only order of magnitude" (10). The data for the life-span have low accuracy due to the poor statistics even for domestic animals (2).

Taking into account the inaccuracy in experimental data, the universality is remarkable: $\delta_1 = 0.014$, $\delta_2 = 0.007$; $\overline{\phi_1} =$

Table 1. Deviations from universality in different taxa of animals

Taxon	δ_3	$\bar{\phi}_3$	γ_3	a_3	$\tilde{\delta}_3$	β_3
Mammals	0.006	0.01	0.08 ± 0.01	4.4 ± 0.3	0.005	−0.01
Birds	0.005	0.01	0.02 ± 0.01	0.6 ± 0.3	0.005	−0.01
Reptiles	0.01	−0.02	0.05 ± 0.02	4.2 ± 0.7	0.01	−0.02
Amphibians	0.01	−0.03	−0.02 ± 0.04	0.4 ± 0.5	0.01	−0.03
Fishes	0.01	−0.02	0.13 ± 0.02	8.3 ± 0.7	0.01	0.01
Invertebrates	0.02	−0.04	0.11 ± 0.03	8.2 ± 0.8	0.01	0.03

$\bar{\phi}_2 = 0.01$. The most complete set of data is available for Φ_3. For mammals, birds, reptiles, amphibians, fishes, and invertebrates, respectively, δ_3 and $\bar{\phi}_3$ are presented in Table 1.

Certain species have anomalously high ϕ. Possibly, they are biologically special [among mammals examples with the lowest ϕ values are the harbor porpoise (*Phocoena phocoena*), the big brown bat (*Eptesius fuscus*), and the nine-banded armadillo (*Dasypus novemcinctus*)]. If they are excluded, the accuracy δ improves considerably.

It is instructive to consider protozoa and bacteria with oxygen metabolism. There the empirical relation (13) for (rather inaccurate) $\dot{V}_O$, which accounts for Eq. **2.8**, reads: $\dot{V}_O \simeq 4 \times 10^{-3} M^{0.75}$. Substituting this $\dot{V}_O$ into Eq. **2.4**, one obtains $A_3 \simeq 0.04M^{0.08}$. A_3 weakly depends on M and yields, by Eq. **2.6**, $|\bar{\phi}_3| \sim 0.1$, which is significantly higher than in the case of many-celled animals. Such is the accuracy of the universality in a mass range of over 18 orders of magnitude, from bacteria to elephants.

Due to fission, under ideal conditions the number n_{pb} of protozoa and bacteria exponentially increases with time t: $n_{pb} \propto \exp(t/\tau_f)$. The fission time τ_f yields the empirical formula (14) $\tau_f \simeq 5 \times 10^7 M^{0.28}$. This average "life-span" of a single cell between divisions is remarkably close to the formula (Eq. **1.1**) $0.1t_l = 4 \times 10^7 M^{0.2}$ for mammals and to $0.1t_l \sim \varepsilon_1 V^{1/3}/M_w u^3 N_O \sim 4 \times 10^7 M^{1/3}$, which follows from Eq. **2.2** divided by Eq. **2.4.** (The similarity between τ_f and $0.1t_l$ is considered later, as well as the meaning of t_O for a single cell. Meanwhile, note the validity of the last formula over 18 orders of magnitude of M.)

The verified universal relations suggest the hypothesis of superuniversality in the distribution of basic energies. The incoming energy, which includes, e.g., basal, nonbasal, and nutrient metabolism, is transformed into the energies of the microscopic (e.g., oxygen atom) intra- and intercellular drift; macroscopic (e.g., blood) flow, heat/entropy production; body surface losses; and chemical reactions. The macroscopic blood flow energy is, by *Section 2*, $\varepsilon_w \sim M_w u^2$ per molecule. According to Eqs. **2.3** and **2.4**, it is ~ the basal energy per body atom per heartbeat $1/\omega_h$ and per time t_O. The higher oxygen concentration in blood yields the oxygen drift into the surrounding tissue. Its velocity is (11) $u_d \sim u_O c$, where $u_O \simeq (3k_B T/M_O)^{1/2} \simeq 10^5$ cm/sec is the thermal velocity of an oxygen atom (k_B is the Boltzmann constant and $T \simeq 300$ K is the thermodynamic temperature) and c is the number of oxygen atoms per blood (mostly water) molecule. The volume concentrations of the oxygen in the air and in the blood are of the same order of magnitude: the former is $c_v = 0.21$ and the latter, due to hemoglobin, reaches (15) 0.2. The blood density is ~1000 times higher than the air density. In blood an oxygen molecule dissociates into two atoms. So, $c \sim 0.2 \times 10^{-3} \times 2 \sim 4 \times 10^{-4}$. Thus, $u_d \sim 40$ cm/sec. The corresponding energy $\varepsilon_d \sim M_O u_d^2$ per oxygen atom (M_O is its mass) is $\sim \varepsilon_w$. Thus, one arrives at superuniversality: All considered basic energies are the same within an order of magnitude for all animals (universality) in all considered processes (superuniversality). This is reminiscent of the energy equidistribution (between degrees of freedom) in physics and seems rather natural physically.

Conversely, superuniversality implies Eqs. **2.3** and **2.4**, and thus Eqs. **2.7** and **2.5**, with no adjustable parameters. Indeed, the oxygen drift velocity u_d is related to the oxygen thermal velocity and volume concentration in the air. By virtue of superuniversality, $M_O u_d^2$ is $\sim \varepsilon_w$ and ~ the basal metabolism per $1/\omega_h$ and t_O. This yields Eqs. **2.3** and **2.4.**

Of course, Eqs. **2.3** and **2.4** imply superuniversality for considered energies only. This raises the intriguing question for experimentalists: is superuniversality valid for all basic biological energies?

Section 4. Implications and Speculations

(*i*) Oxygen consumption (via some products of oxidation, including peroxides and free radicals) yields a by-product—destructive damage to molecules in vital cells. Suppose that superuniversality is valid for destructive energy also. Then, by Eq. **2.2**, its life-span production is related to ~10 oxygen molecules per every body atom on average. A 0.1 fraction of their oxidation energy is $\sim \varepsilon_0 \simeq 4$ eV. (The origin of the factor 0.1 is discussed later.) It is (11) ~ the covalent binding energy in every molecule, and thus sufficient to break key chemical bonds in it. If they are not repaired, the cell will die. The death of vital cells is lethal to an animal. Thus, for all animals the lethal molecular damage energy is ~0.1 of the total basal energy consumption. I speculate that this is not accidental. I suggest as a second main postulate that natural death is related mainly to the irreparable molecular damage to vital cells or molecules (e.g., a DNA or its part), which is a by-product of energy metabolism. [This is consistent with theories which relate aging to various forms of damage to DNA, cells, tissues, and organs (2, 16).] The corresponding destructive energy consumption per atom per lifetime t_l is $\sim 10\varepsilon_0$. Its power is $\sim 10\varepsilon_0/t_l$. Thus the first main postulate of superuniversality yields $\varepsilon_1 \dot{V}_O/N \sim 10\varepsilon_0/t_l \sim \varepsilon_w$—i.e., Eq. **2.2** (where $\varepsilon_1 = N\varepsilon_0$) and Eqs. **2.3** and **2.4.** Thus, the two postulates yield all universal relations with no adjustable parameters.

(*ii*) If natural death is indeed related to irreparable cell damage, then the mortality rate μ depends on the relative number n of undamaged vitally important cells. If their characteristic lifetime is τ, then $dn/dt = -n/\tau$ and $n(t) = \exp(-t/\tau)$. When $n \ll 1$, the "mortality time" $1/\mu$ may be expanded in n: $1/\mu \simeq \tau_2 + \tau_1 \exp(-t/\tau)$, where τ_2, τ_1, and τ are constants obtained from the data; t is age. The most accurate and statistically reliable μ data are available for humans. The Swedish 1987–1991 life tables (17) (for a period when Sweden was neither at war nor had significant immigration/emigration) yield for, e.g., women $\tau_1 = 3.8 \times 10^5$; $\tau = 8.95$; $\tau_2 = 1.14$ years.† According to ref. 17, $t_l \simeq 110$ years. Thus, $\tau \simeq t_l/12$; the data (2, 18, 19) prove it is true for other mammals also. The relation $t_l \simeq 12\tau$, combined with Eq. **2.2**, implies that few oxygen molecules per body atom are consumed per *cell damage time* $\tau \simeq 0.1t_l$. This elucidates the origin of the factor 0.1 in *i* and the formula for the fission time τ_f of protozoa and bacteria: there $\tau_f \sim$ the single cell "lifetime" τ.

Except for young and very old age, $1/\mu \gg \tau_2$, and in agreement with the Gompertz formula (2, 18), $\mu \simeq \tau_1 \exp(t/\tau)$. The mortality rate is related (2, 17) to the relative number Q

†Life tables demonstrate the saturation of $1/\mu$ with age to the *finite* value $\tau_2 = 1.14 \pm 0.2$ years.

of survivors: $\mu \equiv -d\ln Q/dt$. So, $Q \simeq \exp(-\mu\tau)$. As long as $\mu\tau < 0.7$, survivors form a majority. When $\mu\tau$ exceeds 0.7, the population very quickly dies out. The relative number of undamaged cells is $n(t) = \exp(-t/\tau) = 1/\tau_l\mu$. It is $\sim 3 \times 10^{-5}$ when $\mu\tau = 0.7$. This suggests that a tiny fraction of cells/molecules with approximately the same τ is sufficient for survival, while the damage to these specific "death cells/molecules" is lethal for the population.

(*iii*) Dividing Eq. **2.2** by Eq. **2.3**, one obtains

$$t_l\omega_h \sim 10\varepsilon_0/M_w u^2, \quad \varepsilon_0 = \varepsilon_1/N_O. \qquad [4.1]$$

This yields the known relation (2) $t_l\omega_h \sim 1.4 \times 10^9$. Eq. **4.1** implies that the energy $\sim 10\varepsilon_0$ per body atom may be accumulated in $t_l\omega_h$ heartbeats, with the energy $\sim M_w u^2$ per heartbeat per body atom. This calls for an explanation—if indeed the heartbeat $1/\omega_h$ is special for energy consumption, how and why is this so and where is the energy $\sim M_w u^2$ stored? I speculate that the heartbeat is special because the maximal energy is dissipated in flow discontinuities (more accurately, steep gradients), which are implications of the sudden closing of the aortic and pulmonary valves for a *finite* time. [I find it suggestive that according to the Liouville theorem (20), a function which does not change during any *finite* interval must have singularities.] In a solid, the energy may be stored in strains (21). When this energy is sufficiently high, fatigue leads to a sudden fracture (22, 23). The released energy contributes to the damage. "The waters wear the stones" (Job 14:19). One wonders if, how, and where this may happen in a cell.

(*iv*) Consider the best fit of Φ_i in Eq. **2.5** to experimental data according to

$$(\Phi_i - 1)\ln N = \gamma_i \ln N - a_i. \qquad [4.2]$$

The adjustable parameters for Φ_1 and Φ_2 are $\gamma_1 = -0.03 \pm 0.05$; $a_1 = -1.9 \pm 1.2$; $\gamma_2 = -0.01 \pm 0.02$; and $a_2 = -1.6 \pm 0.5$. The corresponding Φ_1 and Φ_2 root-mean-square deviations are $\bar{\delta}_1 = 0.014$ and $\bar{\delta}_2 = 0.007$. The small but nonzero γ_i implies that A_i in Eqs. **2.2–2.4** in some cases slightly depends on a mass M. Therefore, there must exist a scale for M to provide dimensionless A_i. Indeed, universally $a_i \simeq 61\gamma_i$, and $(\Phi_i - 1)\ln N \simeq \gamma_i \ln(M/M^*)$, where $M^* \simeq 3$ kg. The corresponding values of $\beta_i \equiv (a_i - 61\gamma_i)/\ln N$ are $\beta_1 \sim \beta_2 \sim -0.02$. The values of γ_3, a_3, $\bar{\delta}_3$, and β_3 for Φ_3 are presented in Table 1. The accuracy of Fig. 1 demonstrates that α in Eq. **2.8** effectively accounts for the temperature dependence of the destructive energy, heart rate, oxygen concentration in blood, etc.

Within the root-mean-squared deviation accuracy, $\gamma_1 \simeq \gamma_2 \simeq 0$, and thus A_1 and A_2 in Eqs. **2.2** and **2.3** are almost independent of N, while $\gamma_3 \neq 0$ is an important implication of Eq. **2.1.** The nonzero value of γ may be related to mechanical reasons (6): to the branching of blood vessels into a fractal net of capillaries or to the heart rate being imposed mainly by the blood supply to the brain. Replace Eq. **2.1** with

$$\omega_h \sim u/B^{1/3}, \qquad [4.3]$$

where B is the brain volume. For mammals the empirical relation between B and V is (4)

$$B \simeq 0.08V^{0.7} \qquad [4.4]$$

where B and V are in ml. Now Eqs. **2.3**, **4.3**, and **4.4** yield $\dot{V}_O \simeq 0.2M^{0.77}$, in excellent agreement with the empirical Eq. **1.1.** Eq. **4.4** relates the brain volume B to the body surface area $\sim V^{2/3}$ according to $B/\lambda^3 \sim V^{2/3}/\lambda^2$ with $\lambda \sim 600$ μm, where λ is a characteristic size. Eqs. **4.1**, **4.3**, and **4.4** yield $t_l \propto M^{0.23}$, in agreement with the empirical Eq. **1.1** and with the known fact (24, 25) that t_l scales better with brain mass than with body mass. This may be a hint that the lethal molecular damage is related to specific nerve cells (which do not divide; they may not be those responsible for mental activity). A weak dependence of A_i on M and on the animal order, as well as its fluctuations, may also be an artefact, mimicking the impact of other factors, unaccounted for in Eq. **2.5.**

(*v*) If natural death is related to molecular nerve cell damage, then lethal diseases may be manifestations and implications of this damage, just as car damage in a traffic accident may be a manifestation of a driver rather than a car inefficiency.

Section 5. Outstanding Problems and Summary

Problems. (*i*) The universal relations are remarkably accurate, especially if one takes into account the fact that, e.g., fish consume oxygen from water, where its concentration (which is different from that in fish blood) is significantly less than in the air. The value of $\gamma \lesssim 0.1$ in Eq. **4.2** is rather small. Still, an accurate γ value may be significant (see previous section) and should be accurately determined for different animal orders and families. This may suggest its origin and its relation to evolution.

(*ii*) The cell damage time τ is determined by a relatively (compared with t_l) short time span (but calls for a measurement during a time interval) and thus may be established with much higher accuracy than t_l. This may allow one to verify Eqs. **2.2** and **4.1** with t_l replaced by 12τ more accurately and to find out if for a given species they may be accurate enough to account for individual differences (e.g., between a fat or a slim animal, high and low lung volume, etc.) and to provide specific dietary and exercise recommendations [similar, e.g., to Pauling's suggestion (26) that anti-oxidants increase the life-span].

(*iii*) In protozoa and bacteria $t_O \sim V^{1/3}/u$ is $\sim$ the oxygen drift time through a cell, while the fission time τ_f plays the role of the cell damage time τ. This suggests either that fission allows an organism to get rid of a damaged part or that one of the offspring is less fit. It may also suggest clonal aging. (The situation with metamorphosis times t_m in, e.g., insects may be similar, with each of these times playing the role of t_l in the equations for a given form rather than for a species.) The approach presented here may be generalized to plants and bacteria with other kinds of metabolism (nitrogen, CO_2, etc.). The relation of τ_f and t_m to τ, as well as the dependence of the fission time on the oxygen (or CO_2 or nitrogen) concentration, may be an important generalization and a test of the theory. A similar possibility may be provided by the aging of artificially grown cultures of different kinds of body cells under different conditions. Another approach to test the theory may be related to experiments similar to those on the correlation between a truncated erythropoietin receptor and cell death (27, 28).

Thus, the presented universal relations for basic metabolism are remarkably accurate and physically suggestive. This may be an accidental feature of the empirical relations. Alternatively, this may be related to the reasons considered in *Section 4*. The comprehensive answer to the alternative should be provided by further study.

Summary. (*i*) Basal oxygen consumption per body atom is ~ 10 oxygen molecules per lifetime and $\sim 10^{-8}$ oxygen molecule per heartbeat.

(*ii*) Certain basic energies in all animals are the same within an order of magnitude (superuniversality).

(*iii*) Basal metabolism yields universal relations (Eqs. **2.7** and **2.5**) with no adjustable parameters. Their accuracy is a few percent. They suggest that natural death is related to irreparable molecular damage to specific nerve cells whose concentration is very low.

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