

Article

Entropy Stress and Scaling of Vital Organs over Life Span Based on Allometric Laws

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Abstract: Past theories on total lifetime energy expenditures and entropy generation in biological systems (BS) dealt with whole systems, but the recent literature suggests that the total metabolic rate of a BS, \dot{q}_{body} (W) is a sum of product of specific metabolic rate $\dot{q}_{k,m}$ (W/kg of organ k) of each vital life organ, k {k = brain, heart, kidney and liver, or abbreviated as BHKL, and rest of the organ mass (R)} and mass of each organ k (m_k). Using this hypothesis, Kleiber's law on metabolic rate of BS (\dot{q}_{body}) for animals of different sizes was validated. In this work, a similar procedure is adopted in estimating total entropy generation rate of whole human body ($\dot{\sigma}_{\text{body}}$, W/K) as a sum of product of specific entropy generation rate for each organ, $\dot{\sigma}_{k,m}$ (W/{K kg of organ k}) and the organ mass at any given age (t). Further integrating over life span for each organ (t_{life}), the lifetime specific entropy generated by organ k, $\sigma_{k,m,\text{life}}$ (J of organ k/ {K kg organ k}) is calculated. Then lifetime entropy generation of unit body mass, $\sigma_{\text{body},M,\text{life}}$ (J/{K kg body mass}) is calculated as a sum of the corresponding values contributed by all vital organs to unit body mass and verified with previously published literature. The higher the $\sigma_{k,m,\text{life}}$, the higher the entropy stress level (which is a measure of energy released by unit organ mass of k as heat) and the irreversibility within the organ, resulting in faster degradation of organ and the consequent health problems for the whole BS. In order to estimate $\dot{\sigma}_k$ (W/K of organ k), data on energy release rate (\dot{q}) is needed over lifetime for each organ. While the Adequate Macronutrients Distribution Range (AMDR)/Adequate Intake (AI) publication can be used in estimating the energy intake of whole body vs. age for the human body, the energy expenditure data is not available at organ level. Hence the $\sigma_{k,m,\text{life}}$ was computed using existing allometric laws developed for the metabolism of the organs, the relation between

the m_k of organ and body mass m_B , and the body mass growth data $m_B(t)$ over the lifetime. Based on the values of $\sigma_{k, m, life}$, the organs were ranked from highest to lowest entropy generation and the heart is found to be the most entropy-stressed organ. The entropy stress levels of the other organs are then normalized to the entropy stress level (NES_H) of the heart. The NES_H values for organs are as follows: Heart: 1.0, Kidney: 0.92, Brain: 0.46, Liver: 0.41, Rest of BS: 0.027. If normalized to rest of body (R), NES_R , heart: 37, Kidney: 34, Brain: 17, Liver: 15, Rest of BS: 1.0; so heart will fail first followed by kidney and other organs in order. Supporting data is provided.

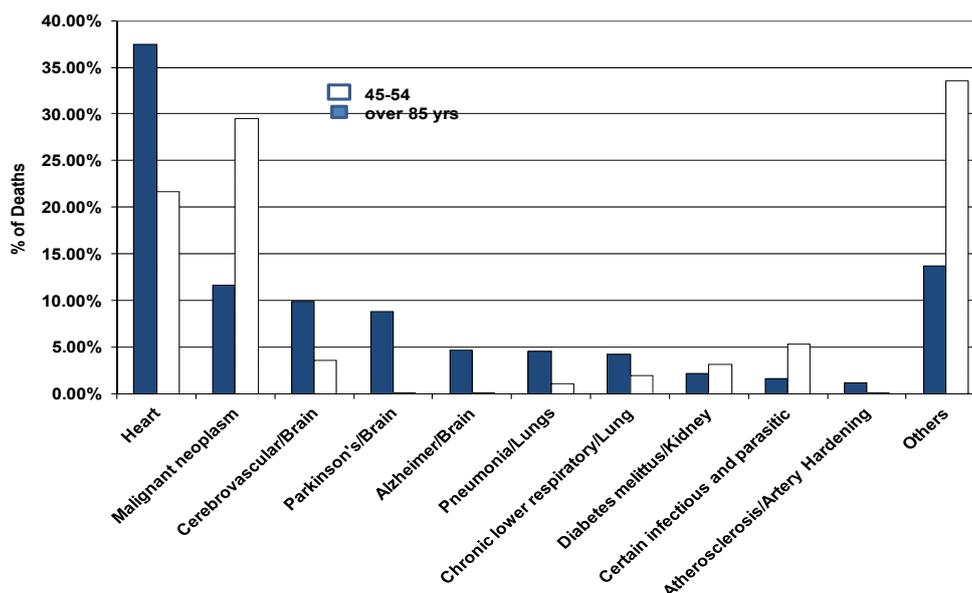
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1. Introduction and Literature Review

The quest for a longer, healthier lifespan of biological systems (BS) ranging from the smallest microbes to the largest mammals and plants is the subject of intensive research and publications. Living organisms constantly need nutrients to generate energy in order to perform vital life sustaining functions including more than one million different types of metabolic reactions driven by the action of enzymes derived from food [1]. The leading causes of natural death in humans are shown in Figure 1. The age related problems include reduction in cardiac (heart), renal (kidney), hepatic (liver), mental/sight/hearing (brain), pulmonary and immune functions; for example, at age 70 the physiological functions including renal functions reduce by almost 50% of those at 30 [3]. This is also consistent with assertion by Schrodinger [4] that “a living organism continually increases its entropy - or, as you may say, produces positive entropy and thus tends to approach the dangerous state of maximum entropy, which is of death”. All potential gradients (e.g., chemical/electric/temperature) which are responsible for sustenance of life or entropy generation cease to exist at death, *i.e.*, cumulative entropy generated over life span reaches a peak value at death. Azbel [5] speculates that natural death occurs due to irreparable molecular damage and a rapid degradation of cellular structures and vital cells like molecular DNA, somehow similar to wear and tear of engines, an indication of process of aging or *thermal denaturation* caused by metabolism during life span. A few of the hypotheses proposed to estimate lifespan are summarized below:

Cell Copy Error Theory (CCE): Under “cell copy error” theory [6], erroneous synthesis of the first set of proteins may lead to more error in second set of proteins leading to accumulation of copying error. Thus, the death is preceded by the constant increase in systemic molecular disorder with loss in physiological functioning of the cells of vital organs such as BHKL [7, 8]. Metabolism is needed to overcome the decay of cells or it is needed to delay the slow death. According to Kirkwood [6], the least value of probability of correct synthesis leads to lethal “error catastrophe” in reproduction of cells leading to “extinction” of living cells. Here, the death of cells occurs via progressive degradation and eventually stopping of re-creation of life sustaining cells. However no quantitative criteria were given to predict the life span.

Figure 1. Leading Causes of Natural Death based on 2001 data (adopted from [2] with permission).



Rate of Living Theory (ROL): This theory is based on the assumption that lifespan specific metabolism of the whole body is constant at 836 MJ/kg [9]. It is based on observation that the BS with a high specific basal metabolic rate (SBMR) has a shorter life span compared to a large BS with lower SBMR and longer life span. It is stated in combustion literature [12] that the heating value of most fuels expressed in kJ per L of required stoichiometric oxygen all nutrients is almost constant (18.5 kJ/SATP-L of O₂, with SATP being 25 C and 1 atm, or 20.2 kJ/CSA L of O₂; see Acronyms). Then, the oxygen used over life span must also be constant at about 45190 SATP-L of O₂ per kg body for all BS. Recently, the Rubner's constant was revised by Spearman to be 590-1100 MJ/kg (excluding man) and 3025 MJ/kg (including man) over species spanning a body mass change of almost 50000 times [10]. Based on the belief that ROL is valid for all BS, the 25 year study on 30% calorie restriction (CR) in rhesus monkeys reported "improved survival" but does not increase the life span [11]. The study seems to suggest that the nutrient composition (e.g., higher % of sucrose, C₁₂H₂₂O₁) and genetics affect longevity more than CR. The leading causes of death are heart disease and were shown to be same in the normally fed and CR monkeys.

Radical Oxygen Species (ROS): This theory proposes that O₂ required for combustion is released as ROS, a by-product of energy metabolism in the mitochondria by phosphorylation processes where electrons are transported. The ROS generated during metabolism may attack cells, result in cell copy error, and cause damage to proteins, lipids and DNA and probably leads to cell death [13]. The ROL theory and ROS model, however, are not necessarily equivalent since metabolic rate and ROS production rate are not always positively correlated; e.g. birds live longer with high metabolic rates [14].

Rate of Entropy Generation (REG): Hershey and Wang [15] estimated entropy generation over human life span using entropy balance but without accounting for diet composition, physical activity level (PAL) and the metabolic efficiencies. The lifetime entropy generation due to metabolic activity was found to be 10,280 kJ/ (kg K) and 11,105 kJ/ (kg K) for females and males respectively.

Modified REG (MREG): The ROL, ROS and REG theories do not account for ATP production during metabolism and its ability to repair damaged cells. It is known from combustion literature that

ROS is proportional to $\exp(-E/\bar{R}T_B)$ where E is the activation energy and \bar{R} the universal gas constant, and hence ROS is body-temperature (T_B) sensitive [12]. A fraction of local energy released is converted into thermal energy resulting in temperature rise and entropy generated while the remainder is used in production of ATP. Note that heat production is necessary to maintain the warm body temperature. The higher metabolic efficiency implies that lesser nutrients are metabolized for the delivery of same work, hence less ROS.

The higher the thermal part of the metabolism reactions, *i.e.*, waste heat, the lower the ATP production, higher the ROS, higher the entropy generation and higher thermal stress and denaturation resulting in faster “ageing”. Thus, the degree of entropy generation is a measure of thermal stress and increased ROS production.

Silva and Annamalai [16] adopted availability concepts, modified REG (MREG) theory by accounting for ATP production and physical activity level, and derived an expression for global entropy generation for the whole body of BS. They estimated specific entropy generation rate of whole body, $\dot{\sigma}_M$, (J/ {kg body K}) as a function of age of the BS, and determined variation specific entropy generation, SEG (J/ {K kg body}) of the whole body of BS with age (t):

$$\sigma_{M,}(t) \left[\frac{J}{\text{kg bodymass K}} \right] = \int_{t_{\text{birth}}}^t \dot{\sigma}_M.(t) dt \quad (1)$$

with $t = t_{\text{life}}$, σ_M , body, life can be estimated.

According to MREG, the natural death of BS is presumed to occur when the whole BS generates fixed amount entropy per unit mass over life span just like Rubner’s hypothesis on fixed energy expenditure. MREG theory is supported by the works of Batato *et al.* [17], Aoki [18,19,20] and Rahman [21] among others, who calculated the entropy generation rate for humans and found it to be within the same order of magnitude as Hershey and Wang and Silva and Annamalai. Higher metabolic efficiency (η) represents better use of nutrients in maintaining the healthy state of organs within BS. Further in support of MREG, pigeons were found to live ten times longer (35 years) than rats (4 years) [22], even though both species have the same mass and hence similar metabolic rates. Walford [23] postulated that the mechanism is related to an increase in η . Apparently it is also attributed to fewer radicals in pigeons (4.6% free radicals) than in rats (16% free radicals) since thermal part of energy is higher in rats. The MREG hypothesis is almost equivalent to REG, ROL and ROS as long as all the ATP is dissipated as heat or when $\eta \rightarrow 0$. The Appendix A.1 includes additional supporting information about Allometric and Scaling Relations.

2. Rationale and Objective

The present paper considers the heterogeneity in heat-producing vital organs of BHKL and the rest of the body mass (R) which makes up the BS, presents the entropy generation of organs using allometric laws to derive the degradation of organs over the lifespan, and accounts for the variation in body weight with age. The amount of specific entropy generation by each vital organ is used as a scale to estimate the stress level, or degree of degradation, of these organs and finally ranks the vital organs in the order of increasing amount of entropy generation (*i.e.*, increased heat contribution). Whichever organ generates entropy at a faster rate per unit mass of organ is under higher entropy (thermal) stress in

the body and hence is presumed to fail first. This approach is similar to the ranking of combustor (45%), boiler (30%) and turbine (10%) in a power generation cycle, where % indicates the contribution to total entropy generated. Note that the ranking is based on the premise that deaths are due to natural causes.

3. Analysis

The analysis is conducted to estimate the following:

- Lifetime energy expenditure (LSEE) and entropy generation (LSEG_k) of each organ k, where k = B, H, K, L and the remainder R
- Specific lifetime energy expenditure, LSEE_M, (kJ/kg body mass) and specific entropy generation, LSEG_M, (kJ/{kg body mass K}) whole body
- The % contribution by the each organ k to the overall energy consumption and % contribution by each organ to the total entropy generation of the whole body.

3.1. Life Span Energy Expenditure of Body in Terms of Energy Expenditure of Vital Organs

If $\dot{q}_{k,m}(t)$ is the specific metabolic rate of organ k, SBMR_k (W/{K kg organ k}) at age (t) and $\dot{q}_M(t)$ is the specific metabolic rate of the whole body (W/kg body), then the life span energy expenditure LSEE_M (J/kg body) is given as a sum of LSEE of each organ using the following expression:

$$LSEE_M \left(\frac{J}{\text{kg body mass}} \right) = \int_{t_{\text{birth}}}^{t_{\text{life}}} \dot{q}_M(t) dt = \int_{t_{\text{birth}}}^{t_{\text{life}}} \sum_k \frac{\dot{q}_{k,m}(t) m_k(t)}{m_B(t)} dt \quad (2)$$

It is noted that the lower case subscript “m” is used for specific quantity of organ k while the upper case subscript “M” is used for the specific quantity of whole body. It is seen that the metabolic energy release rate \dot{q}_k and mass of organ m_k as a function of age (t) are needed for each organ over the life span, in order to estimate LSEE_m. Previous literature measured the difference between oxygen concentration at the inlet and exit of organs, estimated the energy release rate using heating value based on unit mass of oxygen (HHV_{O₂}) consumed, obtained \dot{q}_k (the energy release rate), and related the rate to mass m_k through allometric laws. These laws have been used by Wang *et al.* to estimate metabolic rate of whole body. Following Wang *et al.* [24] $\dot{q}_{k,m}(t)$ can be expressed in terms of body mass using the allometric constants in Table 1 below:

$$\dot{q}_{k,m}(t) \left(\frac{W}{\text{kg organ mass}} \right) = e_k m_B^{f_k} \quad (3)$$

where e_k and f_k are allometric constants for organ k. Calder’s allometric laws for the organ mass to the body mass [25] is given as:

$$m_k (\text{kg organ mass}) = c_k m_B^{d_k} \quad (4)$$

where c_k and d_k being constants for organ k. Equation (3) can also be expressed in terms of organ mass k (Appendix A.1). Expressing m_B as function of m_k , replacing into Equation (3) and multiplying by organ mass m_k , the energy release rate contributed by organ k is given as,

Table 1. Allometric Constants [24,25].

Organ, k	c _k	d _k	e _k	f _k ⁺	W ^{Contrib*}
Brain	0.01100	0.76	21.620	−0.14	11.93
Heart	0.00630	0.98	43.113	−0.12	25.89
Kidneys	0.00893	0.85	33.414	−0.08	23.79
Liver	0.03300	0.87	33.113	−0.27	10.52
Rest, without BHKL	0.93900	1.01	1.446	−0.17	49.2

⁺Recent literature suggests that oxygen accessibility by cells in the organ affects the values of f_k. According to the proposed group combustion theory, smaller organs must have f_k ≈ 0 (isometric law) while the larger organs must have negative values with a limit of f_k ≈ −0.333 [43]. Also the % vital organ masses and SMR decrease with increasing body mass [45].

$$\dot{q}_{k,m}(t) \text{ (W contributed by k)} = c_k e_k m_B^{f_k+d_k} = \left\{ \frac{e_k}{c_k \frac{f_k}{d_k}} \right\} m_k^{\left(\frac{f_k+1}{d_k}\right)} \tag{5}$$

The first 5 columns in Table 1 list the organs c_k, d_k, e_k, and f_k. Wang et al [25] used Calder’s data [26] to predict specific basal metabolic rate (SBMR_k) of organ mass for a 70 kg person including the effect of fat free mass and showed that the computed metabolic rate of whole body with {Σ_k SBMR_k*m_k} yields values similar to those of Kleiber’s allometric model. Elia *et al.* [27] presented the specific basal metabolic rate of vital organ k. Further Gallagher *et al.* [28] measured the mass of the vital organs (m_k) and using Elia’s data, computed the summation {Σ_k SBMR_k * m_k} and showed that the computed resting energy expenditure (REE) is same as measured REE. Finally, using Equations (3) and (4) in Equation (2):

$$LSEE_M \left(\frac{J}{kg \text{ body mass}} \right) = \int_{t_{\text{birth}}}^{t_{\text{life}}} \left\{ \sum_k c_k e_k m_B^{f_k+d_k-1}(t) \right\} dt \tag{6}$$

where the integrand is Kleiber’s law for specific metabolic rate of whole body at any given age, t; thus:

$$SBMR = \dot{q}_M(t) = \sum_k c_k e_k m_B^{f_k+d_k-1}(t) \tag{7}$$

and:

$$BMR = \dot{q}(t) = \sum_k c_k e_k m_B^{f_k+d_k}(t) = \alpha m_B(t)^\beta \tag{8}$$

where the last term represents Kleiber’s law. The coefficients c_k, d_k, e_k, and f_k are presented in Table 1. Since the heating values per unit stoichiometric oxygen are roughly constant (HHV_{O2}) for any nutrient oxidized (see Table 2), the conventional method is to measure the blood flow rates to organs and the difference in oxygen concentration between the arterio-venous blood, and then multiply the oxygen consumption rate by HHV_{O2} in order to obtain the metabolic rate.

Table 2. Thermodynamic Properties of Macronutrients.

Nutrients	Formulae	M, kg/kmol	St.O ₂ , kg/kg	RQ	HHV kJ/kg	HHV _{O2} kJ/kg O ₂	ΔH _c ^o at 37°C MJ/kmol	h _r MJ/kmol	s ^o ₂₉₈ kJ/kmol K	ΔG _c ^o MJ/kmol	$\frac{\Delta G_c^0}{\Delta H_c^0}$	ΔG _M ^o MJ/kmol	ΔS _c ^o kJ/kmol K	Metabol. eff. %
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Glucose	C ₆ H ₁₂ O ₆	180	1.066	1.0	15630	14665	-2815	-1260	212.0	-2895	1.03	-1790	259.5	38.2
Fat	C ₁₆ H ₃₂ O ₂	256	2.869	0.7	39125	13635	-10035	-835	452.4	-9840	0.98	-3125	-630.1	32.2
Protein or Albumin	C ₇₂ H ₁₁₂ N ₂ O ₂₂ S (*1)	1390	2.07	0.8	28893 (*3)	13944		-4480						
Protein	C _{4.57} H _{9.03} N _{1.27} O _{2.25} S _{0.046} (*2)	119	1.54	0.8	22790	14705	-2720	-384		-2665	0.98		-163.8	10.4
Protein [40]	C _{4.98} H _{9.8} N _{1.4} O _{2.5}	117.3	1.413	0.83	19000 [41]	13475								

(*1) [http://en.wikipedia.org/wiki/Basal_metabolic_rate]; (*2) Weighted averages were also used to obtain a surrogated amino acid formula CH_{1.972}N_{0.277}O_{0.492}S_{0.010}, with a molecular weight of 119.39 kg/kmol and a heating value of -2.721x10⁶ kJ/kmol (5.5 kcal/g). kmol based on empirical molecular weight; (*3) Heating value from Boie equation [Chapter 4, ref.12].

3.2. Life Span Entropy Generation (LSEG) in Terms of Entropy Generation of Vital Organs

Using a similar procedure, the cumulative specific entropy generation of each organ from birth to any specific age t is given as:

$$\sigma_{k,m}(t) \left\{ \frac{J}{K \text{ kg of organ } k} \right\} = \int_{t_{\text{birth}}}^t \dot{\sigma}_{k,m}(t) dt \tag{9}$$

where $\dot{\sigma}_{k,m}(t)$ is the specific entropy generation rate of organ k ($=\dot{\sigma}_k/m_k$, W/ {kg organ k·K}). In the current work, the entropy generation of BS is computed as a sum of entropy generation of each organ for a BS which is almost in thermal equilibrium with the immediate surroundings so that the thermal irreversibility is eliminated within organ. This is also consistent with assumption of uniform T within the whole BS in computing lifetime specific entropy generation. At age “t”, the entropy generation rate of whole body in thermal equilibrium, but not in chemical equilibrium within organ k, is given as:

$$\dot{\sigma}_M(t) \frac{W}{\text{kg body mass } K} = \frac{\sum_k \dot{\sigma}_{k,m}(t) m_k(t)}{m_B(t)} \tag{10}$$

where $m_k(t)$ is known in terms of body mass (Equation 4). Using Equation 10 in Equation 1, the cumulative entropy generation of whole BS at age t can be computed.

The total entropy generated is constantly flushed out through bulk heat loss, e.g. perspiration and conduction that occurs throughout the lifespan as long as all organs perform the “vital life” functions.

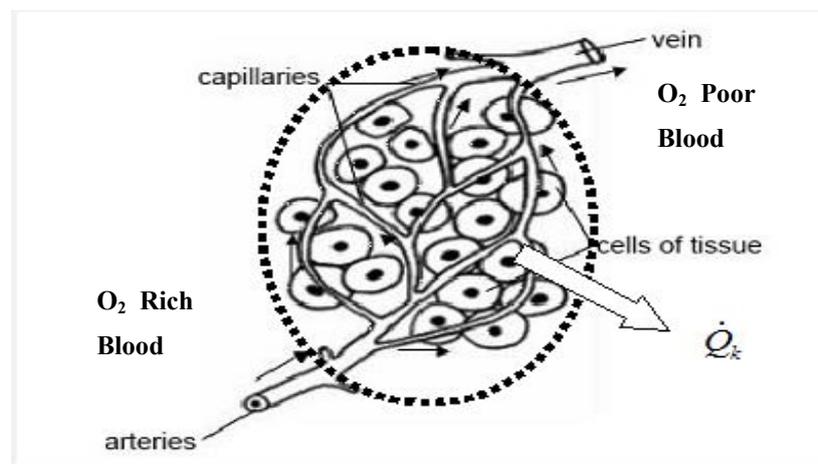
3.3. Availability Analysis

To estimate the lifespan entropy generation of the human BS in terms of entropy generation of each organ, an availability analysis is applied for each isothermal organ. The main nutrient groups are carbohydrates (CH), fats (F), and proteins (P). The metabolic efficiency is (η) same as availability efficiency for an isothermal system in classical thermodynamics literature [28]; for any nutrient n, it is defined as:

$$\eta_n = \left(\frac{\Delta G_{ATP}}{\Delta G_c} \right)_n \tag{11}$$

where $(\Delta G_c)_n$ is the change in Gibbs function of nutrient “n” during metabolism. Typically, macronutrient “n” contains chemical energy at low entropy level (high G_R) (see arteries, inlet to organ k, in Figure 2) while the products (CO_2 and H_2O) have high entropy (low G_P) leaving through veins due to the release of a fraction of energy as heat (\dot{Q}_k) and the remaining fraction as ATP. Due to release of heat, blood remains slightly hotter compared to normal body temperature. Hence typically $(\Delta G_c)_n < 0$. Section 3.3.3 will show that the life span entropy generation (LSEG) depends upon the metabolic efficiency and the life span energy expenditure (LSEE).

Figure 2. Distribution of Nutrients (fuel) to Cells of an organ k; Simplified Schematic (adopted from [31] and modified).



3.3.1. Assumptions

Most of the assumptions are stated in a previous work of Silva and Annamalai [29] and they are briefly summarized below in order to make the present work self-contained:

- The macronutrients or main nutrient groups CH, F and P are modeled using glucose, palmitic acid, and average amino acids composition respectively.
- The η_n , where $n=\text{CH, F and P}$ are different for every nutrient but remain constant over time/age.
- The ATP, which is equivalent to work in thermodynamics, does not create irreversibility.
- Energy requirements are related to body mass $m_B(t)$; statistical data on normal growth of body $m_B(t)$ with age from the Summary Report 2007, US National Center for Environmental Assessment [33].
- Life span of whole species could be defined since the birth and death are well defined; however it is difficult to define the life span of organs. Thus, only extent of degradation of organs is presented in terms of entropy generated during average life span.
- The Gibbs free energy change of nutrients during metabolism, $\Delta G_{c,n}$ is a function of temperature, pressure and mole fraction is approximately same as $\Delta G_{c,n}^\circ$, *i.e.*, $\Delta G_{c,n} \approx \Delta G_{c,n}^\circ$ which implies that nutrients, oxidants, CO_2 and H_2O exists as pure species in the reactants and products.
- In thermodynamic literature, the ratio of $\left| \Delta G_{c,n}^0(T) \right| / \left| \Delta H_{c,n}(T) \right|$ varies from 1.0 to 1.02 for most

hydrocarbon fuels of general formulae C_xH_y when lower heat value is used for the enthalpy of combustion of nutrient n. This is consistent with the findings of Brzustowski and Brena, who

showed that the ratio of fuel availability to lower heat value ranges from 1.04 to 1.07 [32]. When higher heating values are used for the same fuels, the ratio varies from 0.9 to 0.96 for HC and from 0.98 to 1.03 for CH, and F. Hence,

$$\left(\frac{|\Delta G_{c,n}^\circ|}{HHV_n} \right) \approx 1 \tag{12}$$

- (h) While general derivations assume that metabolic efficiency depends upon organ k, age (t) and type of nutrients (j) being oxidized, the quantitative results assume a weighted metabolic efficiency independent of organ k and age (t).

3.3.2. Irreversibility of Organs and Heat Transfer from Organs

As an example, consider the liver: the nutrients (n) along with oxygen and CO₂ carriers enter at inlet (Figure 2), undergo metabolism, a part of the nutrients get oxidized and reduced O₂ and increased CO₂ along with unreacted nutrients exit the organ. Extending the availability analysis of Silva and Annamalai to each organ k, the general availability balance equation is written as [29,30]:

$$\left\{ \frac{d(U - T_0 S)}{dt} \right\} = \dot{Q}_{R,k} \left[1 - \frac{T_0}{T_{R,k}} \right] + \sum_{j, \text{inlet to } k} \dot{m}_j \psi_j - \sum_{j, \text{exit from } k} \dot{m}_j \psi_j - \dot{W}_k - \dot{I}_k \tag{13}$$

$J = \text{CH, F, P, O}_2, \text{CO}_2, \text{H}_2\text{O} \dots; \dot{I} = T_B \dot{\sigma}_k$

where subscripts k refers organ k, j refers to all species including nutrient at inlet of organ k, and $\psi = h - T_0 s$ and T_0 , ambient temperature. It is customary in USA to define $\psi' = \psi - \psi_0$ as stream/flow availability where $\psi_0 = (h_0 - T_0 s_0)$ while in the European Union (EU) it is defined as stream exergy. The $\psi' = (h - T_0 s) - (h_0 - T_0 s_0)$ represents the maximum work that could be delivered by the fluid at given state (T,P) when it is expanded to a dead state (T_0, P_0). The term ψ is called stream availability in EU but there is no parallel definition for ψ in USA. Under steady state conditions one may use either ψ' or ψ in Equation (13) since the term ψ_0 disappears when calculating the difference between inlet and exit availabilities/exergies. For organs within biological systems, $T_0 = T_B, \psi = h - T_B s = g$

Let:

$$\sum_{j, \text{inlet to } k} \dot{m}_j \psi_j = \dot{G}_{R,k}, \quad \sum_{j, \text{exit from } k} \dot{m}_j \psi_j = \dot{G}_{P,k}, \quad \text{and} \quad \dot{G}_{P,k} - \dot{G}_{R,k} = \sum_n \dot{m}_{n, \text{reacted}} \Delta G_{c,n} \tag{14}$$

Using the definition of metabolic efficiency and assumption (f), the ATP work for organ k is given as:

$$\dot{W}_k = - \sum_j \eta_n \dot{m}_{n, \text{reacted}} \Delta G_{c,n} \approx - \sum_n \eta_n \dot{m}_{n, \text{reacted}} \Delta G_{c,n}^\circ, \quad n, \text{nutrients} = \text{CH, F, P} \tag{15}$$

where typically $\Delta G_{c,n} < 0$ for exergetic reactions. Using (14) and (15), quasi-steady state and no thermal energy reservoir and simplifying Equation (13) under steady state:

$$\dot{I}_k = T_B \dot{\sigma}_k = - \sum_n \dot{m}_{n, \text{reacted}} (1 - \eta_n) \Delta G_{c,n}^\circ, \quad n = \text{CH, F, P} \tag{16}$$

The evaluation of irreversibility requires the use of DRI data of the U.S. Food and Nutrition Board on nutrient requirements vs. age at organ level which is not available. Thus, Equation (16) needs to be

simplified further so that one can use allometric laws at organ level to estimate the metabolic rates of each organ. Under assumption (g), the irreversibility rate within each organ k is given as:

$$\dot{I}_k = T_B \dot{\sigma}_k \approx \sum_n \dot{m}_{n,reacted} (1 - \eta_n) HHV_n, \quad n = CH, F, P \quad (17)$$

The term $\dot{q}_n = \dot{m}_{n,reacted} HHV_n$ represents energy release rate due to metabolism of nutrient n, $\dot{q}_k = \sum_n \dot{m}_{n,reacted} HHV_n$ represents energy release rate due to metabolism of all nutrient n within organ k, $\sum_n \dot{m}_{n,reacted} (1 - \eta_n) HHV_n$ represents the difference between metabolic energy release rate and work delivery rate and is a measure of “heat” part of energy released or irreversibility in organ k. The allometric laws for energy release rate can now be used in Equation (17) to estimate irreversibility (J/s) or entropy generate ion rate $\left(\frac{W}{K}\right)$ in each organ. Writing energy release rate in terms of O2 consumed by nutrients “n”:

$$\dot{q}_n = \dot{m}_{n,reacted} HHV_n = \left\{ \dot{m}_{n,reacted} v_{O_2,n} \right\} \frac{HHV_n}{v_{O_2,n}} = \dot{m}_{O_2,n} HHV_{O_2} \quad (18)$$

and:

$$\dot{q}_k = \sum_n \dot{m}_{n,reacted} HHV_n = \dot{m}_{O_2,k} HHV_{O_2} \text{ where } \dot{m}_{O_2,k} = \sum_n \dot{m}_{n,reacted} v_{O_2,n} \quad (19)$$

where $v_{O_2,j}$ is the stoichiometric oxygen mass per unit mass of nutrient j (e.g. for CH, $v_{O_2,CH} = 1.066$ kg per kg of CH), $\dot{m}_{O_2,k}$ the total O2 consumed within organ k, HHV_{O_2} is the heat value per unit stoichiometric oxygen and is approximately constant for most fuels and nutrients. Using Equation (17) entropy generated can be calculated. Table 2 shows properties for macronutrients CH, F and P.

The term $\dot{m}_{O_2,n} HHV_{O_2}$ in Equation (22) represents the energy release rate by nutrient n during metabolism (kJ/kg Of O₂ consumed) and the term $\eta_n \dot{m}_{O_2,n} HHV_{O_2}$ represents the energy used for production of chemical work. Equation (22) suggests that lesser the work you obtain, more the energy available as metabolic heat which results in temperature raise and more thermal *denaturation*. It is apparent from Equation (22) that the heat transfer across the organ results in entropy generation of each organ k.

Similarly from the first law of thermodynamics and under quasi-steady conditions the heat transferred from the organ k:

$$\dot{Q}_k - \dot{W}_k + \sum_{n, \text{inlet to } k} \dot{m}_n h_n - \sum_{n, \text{exit from } k} \dot{m}_n h_n = \dot{Q}_k - \dot{W}_k + \sum_n \dot{m}_{n,reacted} * HHV_n = 0 \quad (20)$$

Using Equation (15) for work

$$\dot{Q}_k - \sum_n \eta_n \dot{m}_{n,reacted} \Delta G_{c,n}^\circ + \sum_n \dot{m}_{n,reacted} * HHV_n = 0 \quad (21)$$

Using the approximation (g) and comparing with Equation (17),

$$\dot{Q}_k \approx \sum_n \dot{m}_{n,reacted} (1 - \eta_n) HHV_n = \sum_n \dot{m}_{O_2,n} HHV_{O_2} (1 - \eta_n) = \dot{I}_k = T_B \dot{\sigma}_k \quad (22)$$

3.3.3. Lifespan Energy Expenditure and Entropy Generation of Organs and Contribution by Organs to the Body

Using Equations (17) and (18):

$$\dot{\sigma}_k = \frac{HHV_{O_2} \dot{m}_{O_2,k} - \sum_n \dot{m}_{O_2,n} \eta_n}{T_B}, \quad n = CH, F, P \tag{23}$$

Metabolic efficiency depends upon the type of nutrient being oxidized, and it is defined by the weighted metabolic efficiency $\{\eta_k(t)\}$ for organ k based on stoichiometric oxygen as:

$$\eta_k(t) = \frac{(\eta_{CH} \dot{m}_{O_2,CH} + \eta_F \dot{m}_{O_2,F} + \eta_P \dot{m}_{O_2,P})_k}{\dot{m}_{O_2,k}} = (\eta_{CH} f_{O_2,CH} + \eta_F f_{O_2,F} + \eta_P m f_{O_2,P})_k, f_{O_2,n} = \frac{\{\dot{m}_{O_2,n}\}_k}{\dot{m}_{O_2,k}}, n = CH, F, P \tag{24}$$

$$\dot{\sigma}_k = \frac{HHV_{O_2} \dot{m}_{O_2,k} (1 - \eta_k(t))}{T_B} = \frac{\dot{q}_k (1 - \eta_k(t))}{T_B} \tag{25}$$

Dividing by the organ mass:

$$\dot{\sigma}_{k,m} \frac{W}{K \text{ kg of organ } k} = \frac{\dot{q}_k \{1 - \eta_k(t)\}}{T_B m_k(t)} = \frac{\dot{q}_{k,m} \{1 - \eta_k(t)\}}{T_B}, \quad \dot{q}_{k,m} = \frac{\dot{q}_k}{m_k(t)} \tag{26}$$

where $\dot{q}_{k,m}$ is specific metabolic rate of organ k.

The LSEG_k of each organ k will be expressed in two forms: i) LSEG_{k,m} of organ k per unit mass of organ k, ii) LSEG_k contributed by organ k to the unit mass of the body. In order to compute LSEG one needs to express $\dot{q}_{k,m}$ in Equation (26) in terms of body mass $m_B(t)$ so that census data on average body weight vs. age (t) can be used and then integrated. As seen in Equation (3), most allometric laws for are expressed in terms of body mass (m_B). Using Equation (3) in Equation (26), the specific entropy generation by each unit mass of organ is given as:

$$\dot{\sigma}_{k,m}(t) \left(\frac{W}{\text{kg organ mass } K} \right) \approx \frac{e_k m_B(t)^{f_k} \{1 - \eta(t)\}}{T_B} \tag{27}$$

Multiplying Equation (27) by organ mass, m_k , and using Equation (4) for organ mass and then dividing by body mass, m_B , one obtains specific entropy generation rate contributed by organ mass m_k to each unit body mass. Thus:

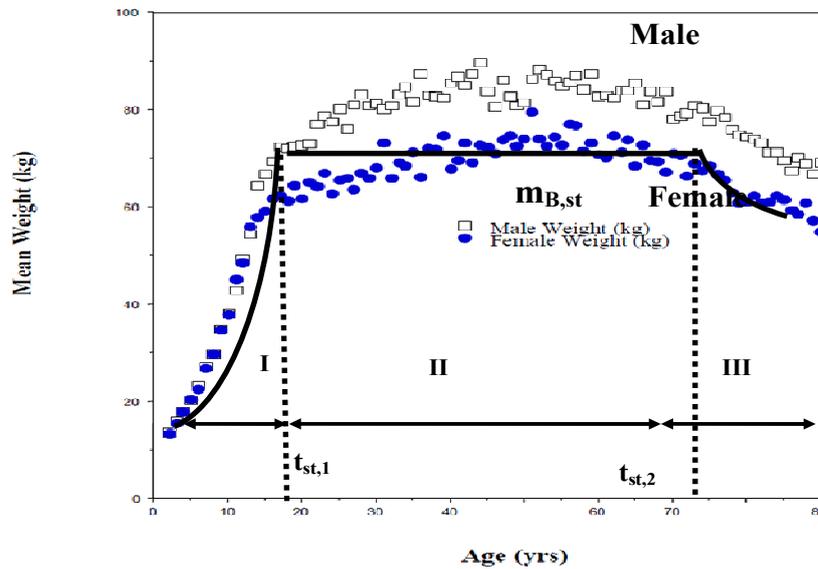
$$\dot{\sigma}_{k,M}(t) \left(\frac{W \text{ due to } k}{\text{kg body mass } K} \right) = \frac{i_k m_B(t)^{j_k-1} \{1 - \eta_k(t)\}}{T_B}, \tag{28}$$

where $j_k = d_k + f_k$ and $i_k = e_k c_k$. It is noted that the entropy contribution rate by organ k to each unit body mass can be obtained just by replacing the allometric constant e_k and f_k in Equation (27) by i_k and j_k-1 [*i.e.*, Equation (28)]. Summing over all organs in thermal equilibrium within the body:

$$\dot{\sigma}_M(t) \left(\frac{W \text{ from BS}}{\text{kg body mass } K} \right) = \sum_k \dot{\sigma}_{k,M}(t) \left(\frac{W \text{ from } k}{\text{kg body mass } K} \right) = \sum_k \frac{i_k m_B(t)^{j_k-1} \{1 - \eta_k(t)\}}{T} \tag{29}$$

Experimental data [33] collected for body mass as a function of age shows three periods of growth (Figure 3).

Figure 3. Curve Fitting Procedure for the Mass Growth and decrease. (Adopted and modified from [33]).



First a period of body mass growth or positive growth, then a second period of almost steady body mass, $m_{B,st}$ and finally, a relative short period of body mass decrease or negative growth. Following the conventional relations typically used in biology, the data was curve fitted with the following allometric form of equation:

$$\frac{m_B(t)}{m_{B,st}} = \left(\frac{t}{t_{st}} \right)^d \tag{30}$$

where $m_{B,st}$ and $t_{st,1}$ are the steady state body mass and the age at which steady body mass is reached respectively. The exponent d is defined as:

$$\begin{aligned} \text{Period I : growth in body mass : } d = c, \quad t_{rst} = t_{st,1}, \quad t_{birth} < t < t_{st,1}, \\ \text{Period II : Steady mass : } d = 0, \quad t_{rst} = t_{st,1}, \quad t_{st,1} < t < t_{st,2}, \\ \text{Period III : decrease in body mass : } d = -c, \quad t_{rst} = t_{st,2}, \quad t_{st,2} < t < t_{life}. \end{aligned} \tag{31}$$

Using Equation (30) in Equation (27), and integrating for the three periods I, II and III:

$$LSEG_{k,m} = \dot{\sigma}_{k,m,life} \left(\frac{kJ}{K \text{ kg of organ mass } k} \right) = \int_{t_{birth}}^{t_{st,1}} \dot{\sigma}_{k,m}(t) dt + \int_{t_{st,1}}^{t_{st,2}} \dot{\sigma}_{k,m}(t) dt + \int_{t_{st,2}}^{t_{life}} \dot{\sigma}_{k,m}(t) dt, \quad k = B, H, K, L, R \tag{32}$$

The net entropy generated over life period (birth to death) = Entropy generated during growth period I + entropy generated during constant mass period II + Entropy generated during mass decrease period III.

The general method of integrating Equation (32) is presented in Appendix A.2. With $\dot{q}_{k,m,st} = e_k m_{B,st} f_k$, one can obtain the specific entropy generated by organ k over lifespan t_{life} as:

$$\frac{T\sigma_{k,m,life}}{t_{st,1} e_k m_{B,st} f_k} = \left\{ \frac{\left[1 - \left\{ \frac{t_{birth}}{t_{st,1}} \right\}^{cf_k+1} \right] (1-\eta_{k,I})}{(cf_k+1)} + (1-\eta_{k,II}) \left(\frac{t_{st,2}}{t_{st,1}} - 1 \right) + \frac{\left\{ \frac{t_{st,2}}{t_{st,1}} \right\} (1-\eta_{k,III}) \left[\left\{ \frac{t_{life}}{t_{st,2}} \right\}^{-cf_k+1} - 1 \right]}{(-cf_k+1)} \right\} \quad (33)$$

For quantitative estimations, $\eta_{k,I} = \eta_{k,II} = \eta_{k,III}$ are assumed to be same as “ η ” for all organs for the three periods and the short period III will be ignored. Thus $t_{st,2} = t_{life}$. Modifying and simplifying Equation (33):

$$\frac{T\sigma_{k,m,life}}{t_{life} \dot{q}_{k,m,st} (1-\eta)} = \left\{ \frac{\frac{t_{st,1}}{t_{life}} \left[1 - \left\{ \frac{t_{birth}}{t_{st,1}} \right\}^{cf_k+1} \right]}{(cf_k+1)} + (t_{st,2} - t_{st,1}) \right\} \quad (34)$$

In order to generalize the results for other lifespan parameters, the left hand side is replaced by “Y” and the right hand side by F. Thus for lifespan specific entropy generation of organ k:

$$Y = \frac{T\sigma_{k,m,life}}{t_{life} \dot{q}_{k,m,st} (1-\eta)} \quad (35)$$

$$F_k(t_{birth}^*, t_{st,1}^*, c, f_k) = \left\{ \frac{t_{st,1}^* \left[1 - \left\{ \frac{t_{birth}^*}{t_{st,1}^*} \right\}^{cf_k+1} \right]}{(cf_k+1)} + (1 - t_{st,1}^*) \right\} \quad (36)$$

where $t_{birth}^* = t_{birth}/t_{life}$, $t_{st,1}^* = t_{st,1}/t_{life}$. Equation (34) is written as:

$$Y = F(t_{birth}^*, t_{st,1}^*, c, f_k) \quad (37)$$

See Table 3, row 2, Column Y for Equation (35) and Column F_k representing Equation (36). If body mass is constant $c=d=0$ and $t_{birth} \ll t_{life}$, then $F(t_{birth}^*, t_{st,1}^*, c, f_k) \rightarrow 1$ and hence from Equation (34), $T\sigma_{k,m,life} \approx t_{life} (1-\eta) \dot{q}_{k,m,st}$, and $\dot{q}_{k,m,st} = e_k m_{B,st} f_k$. Thus the $F(t_{birth}^*, t_{st,1}^*, c, f_k)$ can be interpreted as a growth correction factor to the estimate based on the product of steady entropy generation rate and life span period.

Table 3. Summary of Results for Life Span Parameters.

Parameter	Y	F_k	Remarks
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Life Time Specific Entropy Generation of organ k	$\frac{T \sigma_{k,m,life}}{t_{life} (1-\eta) \dot{q}_{k,m,st}}$	Equation (34)	$\dot{q}_{k,m,st} \left(\frac{W}{kg \text{ organ } k} \right) = e_k m_{B,st}^{f_k}$
Life Time Entropy Generation contribution by organ k to unit mass of body	$\frac{T \sigma_{k,M,life}}{t_{life} (1-\eta) \dot{q}_{k,M,st}}$	Equation (34) with f_k replaced by (f_k+d_k-1)	$\dot{q}_{k,M,st} = c_k e_k m_{B,st}^{(f_k+d_k-1)}$
Life Time Entropy Generation contribution by organ k to whole body	$\frac{T \sigma_{k,life}}{t_{life} (1-\eta) \dot{q}_{k,st}}$	Equation (34) with f_k replaced by (f_k+d_k)	$\dot{q}_{k,st} = c_k e_k m_{B,st}^{(f_k+d_k)}$
Life Time Specific metabolic energy release by organ k	$\frac{q_{k,m,life}}{t_{life} \dot{q}_{k,m,st}}$	Equation (34)	$\dot{q}_{k,m,st} \left(\frac{W}{kg \text{ organ } k} \right) = e_k m_{B,st}^{f_k}$
Life Time metabolic energy contribution by organ k to unit mass of body	$\frac{q_{k,M,life}}{t_{life} \dot{q}_{k,M,st}}$	Equation (34) with f_k replaced by (f_k+d_k-1)	$\dot{q}_{k,M,st} \left(\frac{W}{kg \text{ body}} \right) = c_k e_k m_{B,st}^{f_k+d_k-1}$
Life Time metabolic energy contribution by organ k to whole body	$\frac{q_{k,life}}{t_{life} \dot{q}_{k,m,st}}$	Equation (34) with f_k replaced by (f_k+d_k)	$\dot{q}_{k,st} (W) = c_k e_k m_{B,st}^{f_k+d_k}$

* See Table 1 for $c_k, d_k, e_k,$ and f_k ; lower case subscript “m” per unit mass of organ k, capital ”M” per unit mass of body .

$$\frac{m_B(t)}{m_{B,st}} = \left\{ \frac{t}{t_{St,ref}} \right\}^d, d = c, \quad T_B \dot{\sigma} = \dot{Q} (W \text{ as heat}) = \dot{q} (W \text{ due to metabolism}) (1-\eta), \quad \dot{W}_{ATP} (W \text{ as work}) = \dot{q} \eta$$

As mentioned earlier, the life time entropy generation contributed by organ k to each unit body mass can be obtained just by replacing the allometric constant e_k and f_k in Equation (34) by i_k and j_k-1 . The $LSEE_k$ for each organ k can be estimated as well by setting $\eta_k = 0$ (i.e., all metabolic energy released as heat) in Equation (34). Since metabolic heat contributed by organ k to unit mass of the body is given by $\dot{Q}_{k,M}(t) = \dot{q}_{k,M}(t) * \{1-\eta_k(t)\}$, and since it was assumed that $\eta_k(t)$ remains constant at η_k (assumption h) then multiplying $LSEE_k$ by $(1-\eta_k)$, the life span energy released as heat by organ k ($LSEH_k$) can be estimated. Summing overall organs, the lifetime specific energy released as heat ($LSEH$) of the whole body is obtained. Table 3 summarizes Y for other lifetime parameters of organ k: specific entropy generation by k, contribution to entropy generation of unit mass of body by organ k, contribution to entropy generation of whole body by organ k, metabolic energy release by unit mass of organ k, metabolic energy contribution to unit mass of body by organ k and finally metabolic energy contribution by organ k to whole body. The methodology, presented in Appendix A.2, enables the metabolic and entropy stress level estimation over the life span by just measuring oxygen intake rate into organs and oxygen outflow rate from organs and masses of organs at ages $t = t_{st,1}$ (age at beyond which mass remains constant) and assuming the validity of allometric relations.

4. Results and Discussion

Table 1 presents the necessary allometry data for organ mass and metabolic rate. The data for nutrient properties and the growth data will be presented in the first two sections followed by quantitative results. Organs will be ranked from highest to lowest level of entropy stress or thermal stress. Finally, an attempt will be made to compare the results from the analysis with databases on the causes of normal death.

4.1. Nutrient Data

The properties of CH, F and P and Gibbs free energy data are presented in Table 2. From the data, it is seen that heat released per unit mass of stoichiometric oxygen (HHV_{O_2}) is approximately constant for all three nutrients with an average of 14,335 kJ/kg of O_2 or 18.7 kJ/SATP L of O_2 consumed at standard atmospheric temperature (25 °C) and pressure (101 kPa) (SATP). Note that the medical and biological literature uses 0°C and pressure of 101 kPa (CSA). The entropy generated to energy release ratios for the three nutrients, $\text{ENER} = \{(1-\eta_n)/T_B\}$ are estimated as 0.00219 K^{-1} , 0.00218 K^{-1} and 0.00323 K^{-1} for CH, F and P respectively. Since metabolic efficiencies are almost similar for glucose and fats, the ENER's are similar. The proteins' metabolic entropy is expected to be high due to the low efficiency of the acid cycle transforming proteins to ATP. Thus, thermal denaturation is severe for protein diet metabolism compared to glucose and fat.

4.2. Growth Data

Using UK data on male weight vs. age from 0.83 yrs. to 75 yrs. (see Figure 3 for illustration of curve fitting; actual data from reference 34), a power law curve was fitted [34]. The exponent was set at 0.75 that is close to the exponent used in allometric law for basal metabolic rate. The average error within Period I was about 7.0%.

Period I: $t_{\text{birth}} < t < t_{\text{st, 1}}$, $t_{\text{st, 1}} = 24$ yrs, $m_{\text{B, st}} = 84$ kg, $\{m_{\text{B}}/m_{\text{Bst}}\} = \{t/t_{\text{st, 1}}\}^{0.75}$

Period II: $24 < t < 75$; $m_{\text{B}} = m_{\text{Bst}} = 84$ kg, $t_{\text{life}} = 75$ years

A short period of small weight loss (period III) after 70 yrs and prior to death was ignored.

4.3. Results

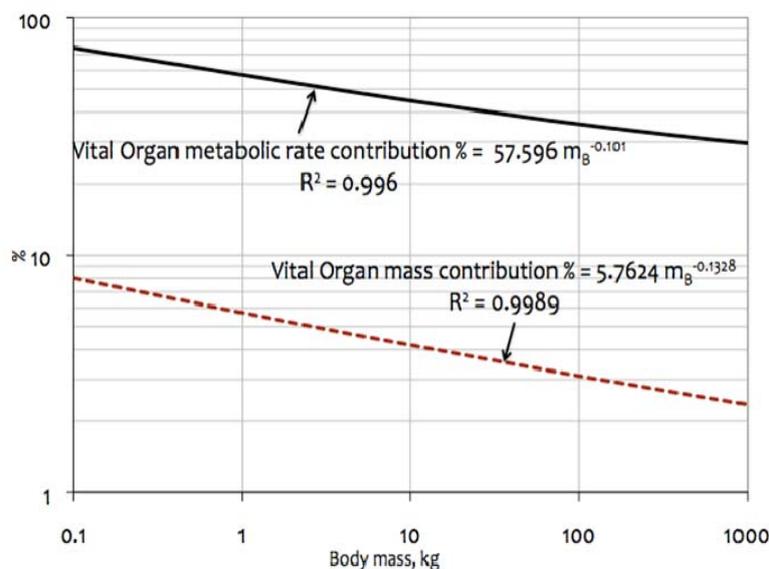
4.3.1. % Contribution by Vital Organs (BHKL) to Overall Metabolic Rates

Summing Equation (4) over organs BHKL and using allometric constants given in Table 1, the organ mass is obtained as a % of total body mass; similarly the BHKL's metabolic rate is expressed as % of total metabolic rate for body mass. Figure 4 shows the results for body mass ranging from 0.1 kg to 1,000 kg was estimate. The fit yields:

$$\% \text{ contribution to mass by the vital organs} = 5.76 m_{\text{B}}^{-0.133} \quad (38)$$

$$\% \text{ contribution to BMR by the vital organs} = 57.6 m_{\text{B}}^{-0.101} \quad (39)$$

Figure 4. Correlation of % of vital organ mass and contribution % by vital organs towards overall metabolism.

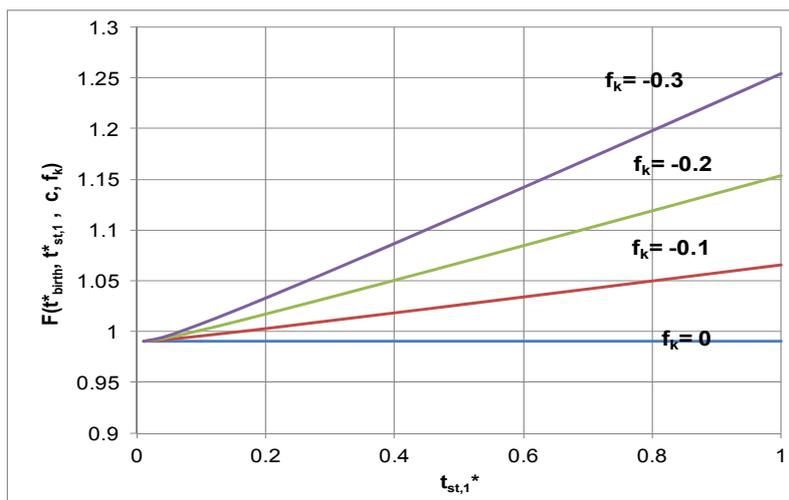


As a check, Equation (38) agrees closely with REE of organs = $56.6 m_B^{-0.07}$ [24]. The % contribution to BMR by four vital organs ranges from 73% for BS of 0.1 kg, 38% for 70 kg human and 29% for a 1,000 kg animal while the % contribution to mass ranges from 8 for BS of 0.1 kg, 3.3% for 70 kg human and 2.3% for a 1,000 kg animal. From the correlation it is seen that the % contribution to BMR and % mass to total mass by vital organs BHKL decrease with age or increase in clock time. The fit is consistent with those of Snyder et al who found that BHKL and spleen organs of most mammals, constituting only about 5% of body weight spend about 60% of whole body REE [35]. It is seen that as the person grows, the vital organ mass % decreases and as such these metabolically active tissues (heart, lungs, brain, liver, and kidneys) contributes less to resting metabolic rate.

4.3.2. Growth Correction Factor, F

Figure 5 plots the variation of growth correction factor $F(t_{birth}^*, t_{st,1}^*, c, f_k)$ for entropy generation with $t_{st,1}^*$ for various values of f_k assuming $c=0.75$. The f_k values cover the range of values tabulated in Table 1. It is noted that SBMR of the body is higher at the time of birth due to high surface area to volume and hence entropy generation rate is higher. As the body weight increases, SBMR decreases and becomes lowest at time of death. If the steady mass is approached slowly (*i.e.*, period I dominant), the period II becomes less and less, $t_{st,1}$ is higher and, $t_{st,1}^*$ approaches unity and hence lifespan entropy generation will be higher. The organs which follow isometric law in metabolic rate must have $f_k=0$; *i.e.*, organ specific metabolic rate is constant over life period and hence entropy generation over life span can be simply given by a product of steady entropy generation rate and life span period.

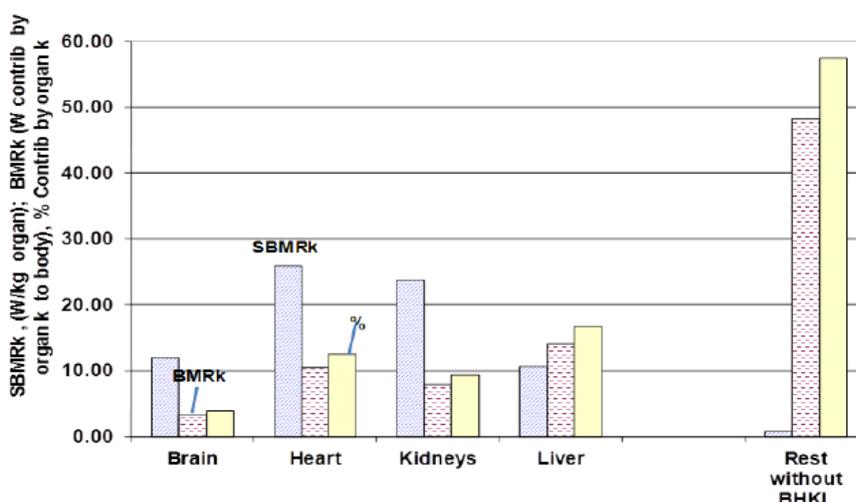
Figure 5. The effect of variation of organ mass growth on correction factor $F(t_{birth}^*, t_{st,1}^*, c, f_k)$ with $t_{st,1}^*$, $c=d=0.75$.



4.3.3. Specific Basal Metabolic Contribution (SBMR_k) by Organ k, $t_{st}^* = t_{st}/t_{life}$

Figure 6 Shows the specific metabolic rate of organ (SBMR_k, hatched lines, W/kg organ), contribution by each organ to the overall specific metabolic rate to the BS (filled with dashed lines, BMR_k, W contributed by organ k /kg body mass) and % contribution to overall metabolism for a 70 kg person. Highest specific metabolic rates (W/kg of organ) occur for heart followed by kidneys, brain and liver. The total metabolic rate for 70 kg person is 84 W out of which 32 W is provided by vital organ having a total mass of 2.3 kg only! In other words, the specific metabolic rates of organs are extremely high compared to overall specific BMR of 1.2 W/kg body mass for BS and as such the cells within vital organs continue to operate under severe stress throughout life span and require constant repair and replacement. The heart has specific metabolic rate of 25 W/kg while rest of the mass (other than BHKL) has specific metabolic rate of only 0.70 W/kg.

Figure 6. Specific Metabolic rate of organs (SBMR_k, W/kg organ mass), W contribution by respective organs (BMR_k) and % contribution to overall metabolism for 70 kg human.



4.3.4. Lifespan Specific Energy Expenditure (LSEE_M)

Tables 1 and 4 present the data used in quantitative estimations. Using Equation (34), the summary of results presented in Table 3, the specific life time entropy generation for each organ and the lifetime overall specific metabolic rate of organ were computed. As a check on the current results, total lifetime energy released per unit mass of body is computed using lifetime metabolic contribution by each organ to unit mass of body. Table 5 shows the results. It is seen that $LSEE_M$ is estimated to be 2832 MJ/kg body mass. Data collected by Speakman indicate $LSEE_M$ of 3025 MJ/kg [10] confirming the validity of current approach. The lifetime entropy generated per unit mass of body is calculated to be 6.3 MJ/{kg body mass·K}.

Table 4. Data for Quantitative Estimations.

% Nutrient consumed for metabolism, CH: F: P =	55:30:15
Computed Fraction of O2 by nutrient “n”, $f_{O_2, n}$. See Equation (24) =	0.349:0.513: 0.138
Average metabolic Efficiency computed by Equation (24) =	31.3%

Age at birth: 0.83, $t_{st, 1} = 24$ years, $t_{st, 2} = 75$ years, $t_{life} = 75$ years, $d=c= 0.75$, Male, $m_{B, st} = 84$ kg

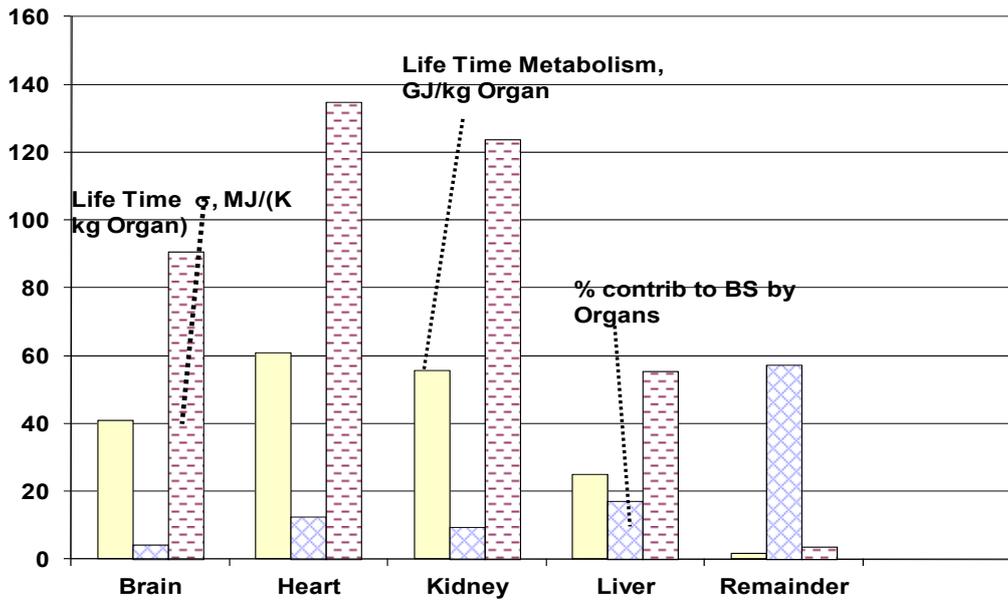
Table 5. Life Span Entropy Contribution by each organ (MJ/kg body mass K) and metabolic contribution (GJ per kg body).

Organ	MJ/(kg body·K)	MJ/kg body
	Sigma contrib.	Metabolic contrib.
Brain	0.252	114
Heart	0.784	352
Kidney	0.589	266
Liver	1.069	480
Remainder	3.610	1620
Sum	6.304	2832

4.3.5. Life Span Organ Entropy Generation

It is noted that CH:F:P split is based on AMDR/AI Data [36].which list the nutrient requirements for adult male or female and it is assumed that nutrients consumed are the same. Figure 7 shows the results for the specific lifetime entropy generated by each vital organ (GJ/kg organ), specific lifetime metabolism (GJ/kg organ) and % contribution by each organ to overall entropy generation of whole BS. It is seen that lifetime specific entropy generation is highest for heart followed by kidneys, brain and liver. Hence the lifetime specific energy released as heat per unit mass of organ will be highest for heart, which will result in highest thermal denaturation process and probably highest amount of ROS species per unit mass of organ that is, the restorability of cells in tissues to the original state is the lowest and therefore vital functions are expected to be impaired first for heart followed by kidneys, brain and liver in order and age old related problem must follow in similar order.

Figure 7. Lifetime Specific entropy generation in MJ/{kg organ·K}, Metabolic Energy in GJ/ {kg organ} and % contribution to entropy by organs to overall entropy generation of BS.

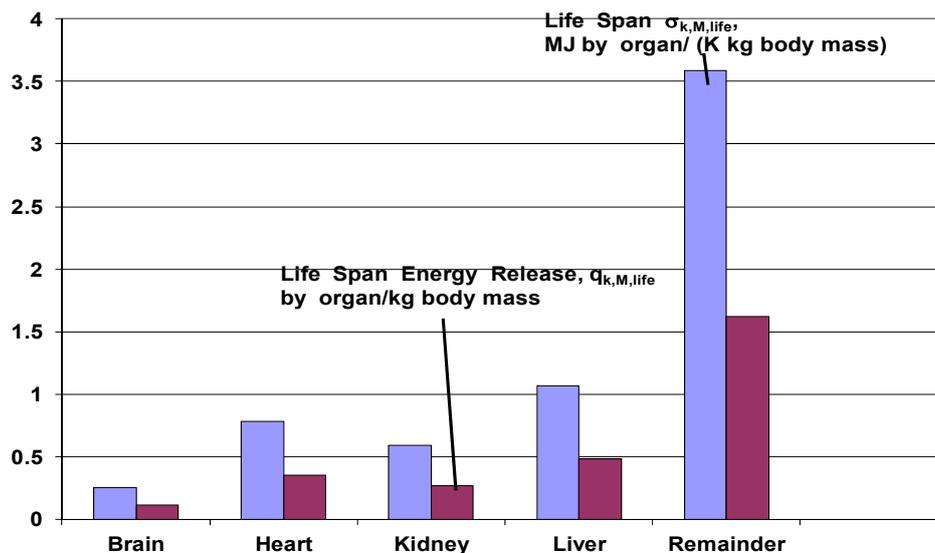


The entropy stress closely follows that of specific life time metabolism since metabolic efficiency (η) was assumed to be constant over life time and similar for all organs due to additional assumption of same % distribution of CH, F and metabolized by the organs. One can define the normalize entropy stress level of organ k (NES) the ratio of the specific entropy generated by organ k to the specific entropy generated by reference organ. If heart is selected as reference organ, the heart-normalized entropy stress (NES_H) values are: Heart: 1.0, Kidney: 0.92, Brain: 0.46, Liver: 0.41, Rest of BS: 0.027. If reference organ is the rest of body (R), then NES_R values are: Heart: 37, Kidney: 34, Brain: 17, Liver: 15, Rest of BS: 1.0; so heart will fail first followed by kidney and other organs in order.

4.3.6. Life span Specific Entropy Generation of Whole Body

The contribution of entropy (MJ/K by organ k per kg body mass) and the metabolic energy (GJ by organ k per kg body mass) by each vital organ k to unit mass of the whole body was also computed. Figure 8 shows the results for both entropy and metabolic contributions by organ k to each unit body mass. It is seen that total lifetime entropy generation is about 6.3 MJ/K per kg body mass (Table 5) with liver contributing the highest for each unit mass of the BS since it constitutes largest % mass within BS, followed by heart, kidney and brain. Without accounting for metabolic efficiency, Aoki [20] plotted entropy generation rate of Japanese male and female individuals ($\dot{\sigma}$, W/K) as a function of age and found that it is dominated by metabolic energy release rate (\dot{q}). Using these plots, the authors estimated the total life span entropy generated for female to be about 392 MJ/K while for male it is estimated to be about 485 MJ/K. The current analysis yields total life time entropy generation as 448 MJ/K.

Figure 8. Lifespan entropy generation {MJ by organ k/ (K kg body mass)} and metabolic heat contribution {GJ by organ k/kg body mass)} by respective organs.



4.3.7. Effect of Nutrients

The previous calculations presume that the metabolized fractions of CH: F: P are same recommended nutrient intake of CH: F: P = 55:30:15 and hence $\eta = 0.31$ (Table 4). The literature suggest that RQ ratio (= CO₂/O₂ moles) is approximately 0.83 under basal condition and reaches as high as 1 for CH [42] during exercise. The contribution to metabolism by CH and Fat is about 97% while the proteins contribute only about 3% [40]. Using the relation for RQ for a mix of X_{CH} moles of CH and $(1-X_{CH})$ moles of fat, one can obtain X_{CH} as [29]

$$X_{CH} = \frac{(23RQ-16)}{(17RQ-10)}, \text{ protein metabolism negligible} \quad (40)$$

With RQ = 0.83 under basal conditions, $X_{CH} = 0.75$, mass fraction of CH = 0.68, and $v_{O_2, stoich} = 1.64$ kg per kg of nutrient mix; using Equation (24), η is estimated as 0.35 which is slightly higher than 0.31 (Table 4). The higher efficiency decreases the estimated lifetime entropy generation only by 6%.

4.3.8. Relation to Life Span

The present analysis seems to suggest the normal death may occur due to impairment of vital functions from the vital organs Brain, Heart, Kidneys, Liver, Spleen (BHKLS) to cite a few. Leading causes of natural death were collected using the data of National Center for Health Statistics and are shown in Figure 2.

More supporting data in the literature follows,

- Looking at data on people living longer than 85 years, heart is cited as #1 cause agreeing with current entropy stress level [2]
- According to current hypothesis, the next organ must be kidney; however cancer is the statistical number 2 cause of death (Figure 2). Recently, Germaine Wong and her colleagues collected data from 3654 Australians within the age group 49–97 years over 10 year period and observed that decreased kidney function leads to an increased risk of developing cancer [38]. Chronic kidney disease is common in people with cardio-vascular disease. Kidney function is

also related to progression to cardio-vascular disease; chronic kidney disease is a risk factor in other chronic diseases such as infections and cancer [38].

- Since ROS concentrations are generally higher with increased T_B (*i.e.*, metabolism which results in fraction of energy converted into heat) and hence, shorter life span, then decreased T_B must lead to prolonged lifespan. “On November 2006, a team of scientists from the Scripps Research Institute reported that transgenic mice which had body temperature 0.3–0.5 °C lower than normal mice indeed lived longer than normal mice.” [39]. Lifespan was 12% longer for males and 20% longer for females. Mice were allowed to eat as much as they wanted. However they had indicated that the effects of such a genetic change in body temperature on longevity are harder to study in humans.
- The third cause happens to be brain as predicted by the MREG model.
- The effect of change in nutrient composition and metabolic efficiency on $\dot{\sigma}_n(t)$ are apparent from Equation (17); when $n = P$, η_n is low (e.g., proteins), and hence $\dot{\sigma}_n(t)$ is higher indicating high protein diet leads to highest metabolic heat and irreversibility. It has been shown by Kapahi and his group that life spans of fruit flies are extended by using low protein diet [37].

The current analysis is based on “oxidative damage” only and presumes that the supply of necessary fuel and oxygen is unhindered throughout lifespan and there is no “fat mass” accumulation throughout the life span both of which are promoted with physical activity/exercise while “heat” damage occurs only in the cells affecting the cell functions. It should be cautioned that it is difficult to attribute the death to a single vital organ failure since the functions are strongly coupled. For e.g., the high blood pressure is linked to kidney disorder along with damages to kidney’s nephrons which then leads to heart attack.

5. Conclusions

- (1) The first and second laws of thermodynamics including availability analyses were applied to the vital organs of biological systems.
- (2) It is shown that the sum of lifetime entropy generation contribution by all the vital organs to each unit body mass is $\frac{6.3 \text{ MJ}}{K \text{ kg body mass}}$.
- (3) The lifetime specific entropy generation of vital organs for 84 kg person is estimated as follows (MJ/ {kg of organ·K}): Brain: 62.4, Heart = 135.4, Kidney: 124.1, Liver: 55.5, Rest of organs: 3.7. The vital organ under most severe stress was found to be heart in agreement with leading cause of natural death.
- (4) The total lifetime contribution by all the vital organs to each unit body mass is $\frac{6.3 \text{ MJ}}{K \text{ kg body mass}}$.
- (5) The heart-normalized entropy stress (NES_H) values are: Heart: 1.0, Kidney: 0.92, Brain: 0.46, Liver: 0.41, Rest of BS: 0.027. If normalized to rest of body (R), NES_R , heart: 37, Kidney: 34, Brain: 17, Liver: 15, Rest of BS: 1.0; so heart will fail first followed by kidney and other organs in order. Supporting data is provided.

- (6) It is possible to estimate lifespan entropy stress just by measuring metabolic rate at the standard weight age (after which weight remains constant), and assuming that allometric laws are valid for organs.
- (7) Since ROS concentrations are generally higher with increased T_B and hence, shorter life span, then decreased T_B must lead to prolonged lifespan.

If the physician monitors the mass growth data vs. age and use allometric laws for metabolic rate, then the current paper presents a method of predicting the vital organ which will fail first; if reliable allometric laws are not available, for more accuracy, one must monitor growth of organ mass (m_k) vs. body mass (m_B) along with their metabolic rates and use these data for ranking the “entropy (or heat) stress” of organs. Future work must be conducted to compare organ-lifespan values of energy and entropy generated for an average individual with those of super-centenarians.

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Acronyms

<i>ADP</i>	<i>Adenosine di-phosphate</i>
<i>AMDR/AI</i>	<i>Adequate macronutrient distribution range/Adequate Intake</i>
<i>ATP</i>	<i>Adenosine tri-phosphate</i>
<i>BHKL</i>	<i>Brain, heart, kidney, liver</i>
<i>BMR</i>	<i>Basal Metabolic Rate</i>
<i>BS</i>	<i>Biological system</i>
<i>CCE</i>	<i>Cell copy error</i>
<i>CDC</i>	<i>Center for Disease Control and Prevention</i>
<i>CH</i>	<i>Carbohydrate</i>
<i>CR</i>	<i>Calorie restriction diet</i>
<i>CSA</i>	<i>Chemist Standard Atmosphere, 0 °C, 101 kPa</i>
<i>DRI</i>	<i>Dietary reference intake</i>
<i>EER</i>	<i>Energy expenditure requirements</i>
<i>ENER</i>	<i>Entropy to Energy Ratio</i>
<i>EER</i>	<i>Estimated energy requirements</i>
<i>HHV</i>	<i>Higher or gross heating value,</i>
<i>HHV_{O₂, n}</i>	<i>higher heating value per unit mass of stoichiometric oxygen of nutrient n</i>
<i>LSEG</i>	<i>Lifetime specific entropy generation (J/kg K)</i>
<i>LSEE</i>	<i>Lifetime specific Energy Expenditure (J/kg)</i>
<i>LSEH</i>	<i>Lifetime specific energy released as heat</i>
<i>ME</i>	<i>Metabolic efficiency</i>

<i>MREG</i>	<i>Modified Rate of Entropy Generation</i>
<i>NES</i>	<i>Normalized Entropy Stress</i>
<i>REG</i>	<i>Rate of Entropy Generation</i>
<i>ROL</i>	<i>Rate of Living Theory</i>
<i>ROS</i>	<i>Radical Oxygen Species</i>
<i>SATP</i>	<i>Standard Atmospheric temperature and pressure (25 C, 1 atm)</i>
<i>SBMR</i>	<i>Specific Basal Metabolic Rate, (W/kg K)</i>
<i>US FNB</i>	<i>US Food and Nutrition Board</i>
<i>VLSF</i>	<i>Vital life sustaining functions</i>

Nomenclature

E	Energy, kJ
F	Growth Correction factor
G	Gibbs free energy, kJ
h	Enthalpy, kJ/kg
I	Irreversibility I, kJ
\dot{I}	Irreversibility rate, kJ/s
m	Mass, kg
m_B	Body mass
m_k	Mass of organ k
\dot{m}_k	Mass flow rate of nutrient n in organ k
$\dot{m}_{O_2,n,k}(t)$	Consumption rate of oxygen by nutrient n in organ k
P	Protein
Q	Heat
\dot{Q}	Heat transfer rate due to metabolic heat release \dot{q}_k at organ k
$\dot{q}_{k,m}$	Specific metabolic energy release rate from organ k per unit mass of organ k
$\dot{q}_{k,M}$	Energy release rate of organ k contributed to the unit mass of body
S	Entropy, kJ/ K
s	Specific Entropy, kJ/kg K
T_B	Body temperature, K
t	Time or age
t_{st}	Time to reach steady weight
U	Internal energy
W_k	Work delivered by metabolism at organ k
$\Delta \bar{G}_C^\circ$	Gibbs free Energy for combustion
$\Delta \bar{G}_M^\circ$	Gibbs free Energy for metabolism (with ATP production)
$\Delta \bar{G}^\circ_{ATP}$	Gibbs free energy

Greek Symbols

η	metabolic efficiency
σ	Entropy generation, kJ/K
$\sigma_{M,k}$	Entropy contribution to unit mass of body by whole organ k
$\dot{\sigma}_M$	Entropy generation rate per unit body mass (W/kg body mass K)
$\dot{\sigma}_{m,k}$	Specific entropy generation rate of organ k (W/{K kg of k })
Ψ	Stream availability, kJ/kg
$\nu_{O_2,n}$	Stoichiometric oxygen mass per unit mass of nutrient n
$\eta_{n,k}$	metabolic efficiency of nutrient n in organ k

Superscript

0	Atmospheric conditions
$B_{,ref}$	Reference mass for body
C	Combustion
k	Organ k
life	Life Span
m	Specific referring to unit mass of organ
M	Specific referring to unit mass of body
n	Nutrient (n)
$P-R$	Difference of value from products to reactants
J	Nutrient j
P	Products
R	Reactants
St	Steady

General Notes

A bar (-) on top of any property indicates its specific property per kmole of substance

A dot (.) on top of any property indicates its time rate of change

Appendix

A1. Alternate Allometric Relations

Most of the previous allometric laws for specific metabolic energy release rates of organs are given in terms of body mass {Equations. (3) and (4)}. Instead, the laws can also be expressed in terms of organ mass m_k . Solving for m_B in terms of m_k from Equation (4) as $m_B = \{m_k/c_k\}^{1/d_k}$ and using in Equation (3), one can obtain allometric laws in term of organ mass m_k as

$$\dot{q}_{k,m} \left(\frac{W}{\text{kg organ mass}} \right) = \left\{ \frac{e_k}{c_k \frac{r_k}{d_k}} \right\} m_k \left(\frac{r_k}{d_k} \right) \quad (a)$$

The contribution of organ k to energy release rate of whole body can be found by multiplying Equation (a) by m_k , and it is given as:

$$\dot{q}_k (W \text{ contributed by } k) = \left\{ \frac{e_k}{c_k \frac{f_k}{d_k}} \right\} m_k \left(\frac{f_k}{d_k} + 1 \right) \tag{b}$$

Alternately multiplying (3) by m_k and using Equation(4), one can re-express metabolic energy release rate contributed by k to the hole body as:

$$\dot{q}_k (W, \text{ contributed by } k) = c_k e_k m_B (t)^{f_k+d_k} \tag{c}$$

Summing over all organs k , Kleiber’s law is written as:

$$\dot{q}(t) = \alpha m_B(t)^\beta = \sum_{k=B,H,K,L,R} c_k e_k m_B(t)^{f_k+d_k} \tag{d}$$

Equation (d), yields Kleiber’s law with \dot{q} in W , $\alpha = 3.252$, and $\beta = 0.76$ [25] which are close to Kleiber’s constants for the whole body with $\alpha=3.391$, $\beta = 0.75$.

A2. Integration:

Consider the expression

$$y(t) = a x(t)^b, \tag{A}$$

$$\text{where } x(t) = c t^d \tag{B}$$

Integrating Equation (A) with time using Equation (B),

$$z(t_2) - z(t_1) = \int_{t_1}^{t_2} y(t) dt = \int_{t_1}^{t_2} a \{x(t)\}^b dt \tag{C}$$

Then it can be shown that

$$z(t_2) - z(t_1) = \frac{t_2 y(t_2) - t_1 y(t_1)}{db + 1} = ac^b \left\{ \frac{t_2^{db+1} - t_1^{db+1}}{db + 1} \right\} \tag{D}$$

Replacing $y(t)$ (which is specific entropy generation rate of organ k) by Equation (27) and $x(t)$ (which is body mass), by Equation (30)

$$z(t_2) - z(t_1) = \left[\frac{t_2 * \text{Spec.Organ Ent Gen rate at } t_2 - t_1 * \text{Spec.Organ Ent Gen rate at } t_1}{\{f_k d + 1\}} \right] \tag{E}$$

$$z(t_{life}) - z(t_{birth}) = \int_{t_{birth}}^{t_{life}} y(t) dt = \int_{t_{birth}}^{t_{st,1}} y(t) dt + \int_{t_{st,1}}^{t_{st,2}} y(t) dt + \int_{t_{st,2}}^{t_{life}} y(t) dt \tag{F}$$

which is similar to Equation (33).

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