Article

Entropy Generation and Human Aging: Lifespan Entropy and Effect of Physical Activity Level

Carlos Silva and Kalyan Annamalai *

Department of Mechanical Engineering, Texas A&M University, College Station, Texas 77843-3123, USA; E-mails: cas@tamu.edu; kannamalai@tamu.edu

* Author to whom correspondence should be addressed.

Abstract: The first and second laws of thermodynamics were applied to biochemical reactions typical of human metabolism. An open-system model was used for a human body. Energy conservation, availability and entropy balances were performed to obtain the entropy generated for the main food components. Quantitative results for entropy generation were obtained as a function of age using the databases from the U.S. Food and Nutrition Board (FNB) and Centers for Disease Control and Prevention (CDC), which provide energy requirements and food intake composition as a function of age, weight and stature. Numerical integration was performed through human lifespan for different levels of physical activity. Results were presented and analyzed. Entropy generated over the lifespan of average individuals (natural death) was found to be 11,404 kJ/ºK per kg of body mass with a rate of generation three times higher on infants than on the elderly. The entropy generated predicts a life span of 73.78 and 81.61 years for the average U.S. male and female individuals respectively, which are values that closely match the average lifespan from statistics (74.63 and 80.36 years). From the analysis of the effect of different activity levels, it is shown that entropy generated increases with physical activity, suggesting that exercise should be kept to a "healthy minimum" if entropy generation is to be minimized.

Keywords: Biothermodynamics, Metabolism, Entropy, Entropy generation, Human lifespan, Aging, Biological system

1. Introduction

The biosphere, a thin layer around earth, contains all living species including plants, and all the living organisms owe their existence to atmosphere (air), hydrosphere (water) and lithosphere (land). The quest for a longer, healthier lifespan of biological species (BS) is the subject of intensive research and publications [1, 2, 3]. Energy is the capacity to transfer energy in the form of work (climbing a hill) to heat (cooling in a cold weather). Plants are producers of chemical energy (autotraphs which produce organized molecules from disorganized CO2, H2O) while the primary biological species (heterotraphs) are consumers of energy produced by autotraphs. Living organisms constantly need to expend energy to perform vital life functions. This includes running the heart, operating the neural computer (brain), performing mechanical functions (e.g. lifting weights, walking, etc), and eating food to maintain body temperature in the presence of heat loss to the environment, driving other chemical reactions, replicating, and repairing tissues and removing wastes. This energy is provided by oxidation of organic substances called metabolism: carbohydrates (CH), fats (F) and proteins (P) introduced to the organism by feeding. But what are the principles relating energy and metabolism with life span?

While the first law of thermodynamics deals with conservation of energy where total energy is conserved (e.g. energy of organisms + energy of surroundings which include the rest of the universe), the second law states that the irreversible processes occur due to property gradients: mass transfer by concentration gradient, heat transfer by temperature gradients (e.g. temperature difference between sun and the leaf in a plant in the biosphere which supplies heat for the photo-synthesis process resulting in energy transformation from the thermal form to chemical form), momentum transfer by velocity gradients, and life sustaining chemical reactions due to chemical potential gradients called Gibbs function. The BS must also obey the laws of thermodynamics just like heat engines. However, the BS is a bio-engine which converts a part of the chemical energy of food into another form of chemical energy stored in ATP molecules (called the "work currency" in bio-chemistry). The ATP also serves as reaction currency to drive non-spontaneous processes by chemical coupling just as the sun provides energy for the photo-synthesis process.

Using the first law, the quantity of nutrients metabolized by an organism, hence its energy input, can be estimated by measurements of inhaled O_2, exhaled CO_2, and the knowledge of the chemical composition of food intake. The metabolic energy input varies depending upon resting conditions, the basal metabolic rate (BMR) and the extent of physical activity level (PAL). If two experiments are performed on the same organism, the first one in resting condition (BMR) while the second one is performing some measured work (PAL), the difference in the amount of food metabolized $\dot{Q}_{Chem,PAL}$ and $\dot{Q}_{Chem,BMR}$ (second and first cases) can be expressed as energy input for conversion to work and compared to the work output ($\dot{W}$) in order to obtain the metabolic work efficiency (MWE). These experiments have confirmed that the efficiency of muscular work is fairly consistent 25-30 percent [4].

Species with larger mass and surface areas generally require more heat generation than smaller ones so the metabolism is typically expressed on a unit mass basis. If life span specific metabolism or specific energy expenditure (LSEEm, kJ/kg) is a constant, as assumed by Rubner [5a], then the energy consumption model also known as *the "rate of living" theory [ROL, 5b]* can be adopted to predict life span; this model shows that life span is proportional to the body mass to a power of 1/3. *The ROL is*

somewhat analogous to faster breakdowns of cars, machines, etc., if one uses them frequently and more intensively. The same theory might be applicable to animal (and human) life.

The irreversible processes occurring between biosphere, atmosphere, hydrosphere and lithosphere as well as the irreversible chemical and thermal processes within BS result in entropy generation (σ), and the generation ceases once the gradients disappear. Unlike "s", σ is not a property. For e.g., the metabolic reactions within BS of specified mass m resulting in energy release are highly irreversible thus, generating entropy which tends to accumulate within a biological system (BS); however the generated entropy is constantly flushed out through mass out as long as life exists. If not flushed, the "s" (a property) will increase with time with corresponding change in T and P and vice versa. The flushing of σ requires work by BS which is produced by the conversion of chemical energy into work. When chemical potential gradients within BS cease to exist, life sustaining chemical reactions can not occur. Hence, there is no more entropy generation and death eventually occurs. As the life progresses, one can estimate specific entropy generation rate $\dot{\sigma}_m$ ($=\dot{\sigma}/m$, kW/kg-K), track the $\dot{\sigma}_m$ (t) of any biological system (BS) with time and estimate the life span entropy generation per unit mass (LSEGm; kJ/kg-K):

$$\sigma_m(t) = \int_0^t \dot{\sigma}_m(t)dt$$

With t = t_{life}, $\sigma_{m,life}$ can be estimated. If LSEGm= $\sigma_{m,life}$ (kJ/kg-K) and the average $\dot{\sigma}_m$ is a constant throughout a life span as assumed by Annamalai and Puri [6,7] then such a model seems to yields a relation qualitatively similar to that of Rubner. More details are provided in later sections.

The current model proposes an entropy generation ($\dot{\sigma}_m$) concept and presents an estimate of $\dot{\sigma}_m$ (t) during the human lifespan. The model includes the various constituents in the nutrients, age related body size and mass, physical activity levels, and more importantly, metabolic efficiency. The results were based on data from the Food and Nutrition Board and the Center for Disease Control and Prevention. Nutrient consumption and energy expenditure vs. age are presented for both average male and female individuals. Prior to proceeding with a rigorous analysis, a brief literature review is presented.

2. Literature Review

2.1 Allometry

Biology literature uses allometric laws to describe the relationship between various parameters of growth or processes in living organisms. For example, the general equation:

$$y = a\, x^b \tag{1}$$

can be used to express the following:

a) *Metabolic rates:* Metabolism involves oxidation of glucose, fats and proteins in the nutrients, which require oxygen for oxidation. The O_2 consumption rate is given by the above general law [8] with:

   y= O_2 consumption rate in mL/hr, x= mass of body in g

   a= 4 - 4.2, b = 0.68

Hofman [9] reports:

$a = 0.064$, $b = 0.734$ with $y = mL\ O_2/min$ and $x = $ body mass in g

Schmidt-Nielsen [10] presents:

$y =$ specific metabolic rate (W/kg), $x =$ mass of body in kg

$a = 3.55$, $b = -0.26$

b) Mass of brain: Same equation (1) with:

$y = $ brain mass in g, $x = $ body mass in g

$a = 0.043$, $b = 2/3$ to 0.73

c) Body surface area (BSA) [http://ajpendo.physiology.org/cgi/content/full/281/3/E586]

y, BSA in m^2, x, body mass in kg

$a = 0.1173$, $b = 0.6466$, $R^2 = 0.9914$

For *Lifespan,* a more complex relationship is observed:

$$y = \alpha\ x^c\ z^\beta \qquad\qquad\qquad\qquad\qquad (2)$$

$y = $ lifespan, days

$x = $ body mass in g

$z = $ brain mass in g

$\alpha = 23$, $c = 0.6$, $\beta = -0.0267$ (declining rate attributed to less neuron density with increasing size [9])

One of the allometric scaling key equations is the Metabolic Scaling theory relating metabolic rate to body mass [11, 12]. Under the constant specific metabolism or constant energy expenditure assumption, the said theory would predict life span; however, the validity of the theory is highly debated. Even though the simple exponential equation seems to match data from a large number of species with a wide range of sizes and metabolic rates, the value of the exponent arising from the curve fit (usually ¾) does not include terms for metabolic efficiency or temperature, which makes for a weak argument. However, the works of Payne et al. [13] and Thonney et al [14] on metabolic requirements for dogs show a clear scaling with adult weight to the power of 0.67 and 0.876 respectively. The *Nutrient Requirements for Dogs* [15], published by the National Research Council recommends a scaling with adult dog weight to the power of ¾, which is the relationship currently used in research on dog nutrition.

Experiments on caloric restriction diets have shown that reduced metabolism results in increased lifespan of mice and other species, generating alternative theories like the one from Demetrius et al [16] accounting for metabolic efficiency. Opponents to this theory argue that the required metabolic efficiencies needed to reach the known curve fit exponents of metabolic scaling are too high (> 80%) when compared to well known laboratory values (from 15 to 45%). There are many complex factors that need to be accounted for and cannot be captured by a simple equation. Supporters of the metabolic scaling argue that organisms naturally evolve into configurations that maximize efficiency/reduce entropy. Maximum efficiency is a desired principle for living organisms; therefore, the majority of the species naturally fall into a very narrow range of the metabolic scaling. For example, the Constructal Design Principle proposed by Bejan et al. [17, 18, 19] shows how optimal geometric forms for fluid and heat flow have dissipation which scales to the ¾ power of their size, predicting how natural

occurring structures (tree branches, river deltas, vascularized tissue, lightning) repeat themselves due to the entropy minimization principle.

2.2 Lifespan

The life time volume of blood pumped by the heart is approximately 200 million L/kg of the heart while the total number of beats is approximately 1.1 billion per lifetime [20]. Azbel [21] speculates that natural death occurs due to irreparable molecular damage and a rapid degradation of cellular structures (mitochondria) and vital cells like molecular DNA, similar to wear and tear of engines, an indication of process of aging caused by metabolism during life span. Here, the death of cells occurs via progressive degradation and eventually stopping of re-creation of life sustaining cells. In 1908, Rubner [5] noted that food intake per gram decreased with an increasing life span among five domestic animals (guinea pig, cat, dog, cow and horse). He calculated the energy intake per gram per life span (LSEEm) and found that the variation in LSEEm between species was small (1, 5 fold), although the variation in body mass was very large. Including data for men, the variation in life-time energy expenditure was slightly larger, but still only 5 fold. Rubner estimated the lifespan energy expenditure (LSEEm) to be about at 836 MJ/kg body and concluded that mass-specific energy metabolism times the maximal lifespan was a constant. Spearman [22] reported that the life time energy ranges from 590MJ/kg to 1,110 MJ/kg (excluding man); it extends to 3,025 MJ/kg, including man. It is apparent that energy expenditure changes only 5 fold while body mass changes by 50,000 times. Recently using data on the breathing rate of air per hr (360 L/hr) and the average life span of 75 years {CDC data for men} with an average body mass of 75 kg, the metabolic rate and total life time energy were estimated as 70 W and 2,210 MJ/kg [6]. Thus, presumably based on ROL, the "prolongevists" promote low carbohydrate diets and vitamins (low calories), while spiritual healers and yogists appear to promote lowering the rate of metabolism. There are some deficiencies in the constant energy requirement hypothesis [23]. Many times basal metabolic rates (when fasting and resting at thermo-neutral temperatures) have been used to estimate life time energy expenditures. *Basal metabolic rate (BMR) contributes only 40% to the total estimated (daily) energy requirements (EER) and does not account for activity levels. Further, the analysis does not account for energy to perform life sustaining functions. Spearman used a residual energy (Residual =EER-BMR) expended model to account for activities and the model suggests that the energy per unit mass is not independent of body mass m.*

The earliest work on entropy estimation for human lifespan was performed by Hershey [24] and Hershey and Wang [24, 25]. The reasoning is that for a human in resting condition, most of the energy output from the metabolism of food appears as heat, and neglecting other causes of irreversibility, they approximated the internal entropy production (generation) rate by the BMR divided by the average body temperature and estimated the entropy exchange with the surrounding by the change of entropy in the breathing air.

Hershey and Wang's work defined several useful concepts like entropic age, expected lifespan and senile death. Their work suggests that it is not the total entropy during lifespan, but the rate of change on entropy production that defines the senile death, that is, once (ds/dt) reaches zero. This theory of aging has been referred to as Thermal Denaturation. Their calculations indicated that a lifetime accumulation of entropy production was 10,025 kJ/kg_K (2,395 kcal/kg_K) for human males and

10,678 kJ/kg_K (2,551 kcal/kg_K) for females. The lifetime entropy production (or internal entropy) due to metabolic activity was found to be 10,280 kJ/kg K (2,456 kcal/kg_K) and 11,105 kJ/kg_K (2,653 kcal/kg_K) for males and females respectively. The difference between total and internal entropy was the exchange with the surroundings, which was considered negative because air is returned to the environment at conditions (temperature and molar fraction) different from equilibrium.

However, a couple of deficiencies should be highlighted: *i) they used BMR to estimate body entropy generation, and BMR is a resting metabolism which can differ significantly from actual (field) metabolic rates, where levels of physical activity are accounted for. ii) The effect of the diet composition on the entropy generation was not studied.*

Batato et al [26] presented a second law analysis in which a model of the human body was established with several constituents (fat, muscle, bone, etc.) and body temperature using a Nuclear Magnetic Resonance device. Metabolism rates were obtained by the levels of oxygen consumption and carbon dioxide production in the individuals, assuming the nutrients metabolized were CH, F and P. They proposed that entropy generation in the human body can be divided in 3 stages: during growth (childhood) the rate of entropy generation decreases; for a healthy adult, this value approaches zero (questionable since ds/dt can be zero, but not $\dot{\sigma}$); and during old age, until death, the rate of entropy generation is positive. The work was focused on the entropy of individuals in stage 2, where entropy generation due to internal irreversibility was assumed to be zero, and *all the entropy generated was due to heat transfer*, nutrient absorption, refuse rejection, etc. The estimated entropy generation per kg of body mass is about half of the value presented by Hershey and Wang. *The data is too narrow-ranged to extrapolate over long periods of time*.

Annamalai and Puri [6] used the first law analysis to obtain the metabolic scaling law for BS, and then used the second law to estimate $\dot{\sigma}$, and assumed it to be constant for a 70 kg average person. They predicted life span as 77 years assuming $\sigma_{m,max}$ as 10,000 kJ/kg_K. Although this calculation is simplistic, its values seem reasonable when compared to statistical data, and most importantly, yielded a scaling law for life span with mass for all BS.

3. Rationale and Objective

The literature presented an overview of previous models for predicting entropy and the lifespan of species based on allometric scaling laws. It was apparent that the *LSEE model ignores the effects of life sustaining ATP production while the current model accounts for a part of energy conversion to ATP*. The glucose oxidation with a heating value (HV) of 15,630 kJ/kg converts 32% of heat of reaction into work (production of *ATP molecules*) while protein, with an HV of 22,790 kJ/kg delivers only 10% as work [27]. The remainder of the heat of reaction is disposed off as heat and building body substance. Further, the life span prediction based on energy consumption does not depend upon whether intake is through CH, fat, or protein (and hence, their metabolic efficiency). The current entropy generation concept which accounts for ATP production is an improvement over energy concept and accounts for dependence of entropy generation rates on metabolic efficiency, and the ration fed to BS. It is known that the ration changes from species to species. For e.g., a dairy cow is given different rations for producing more milk compared to the feedlot cattle for producing more "meat". The present concept of life span for BS *is analogous to the breakdown of machines as in energy concept, but with a*

difference; a part of energy is used to repair and tune up the machine, extending the life span. In this case, the production of ATP serves such a purpose.

The current analysis based on the entropy generation concept considers the following:

1. Accounting for the metabolic efficiency (production of ATP) in the BS. We will start with the basic chemical reactions typical of metabolism to determine the efficiency of ATP production, or MWE, for each of the three main nutrient groups. In the BS, energy not converted to ATP is disposed of as heat, thus, increasing entropy.

2. Accounting for the effects of age, body mass, physical activity level and diet composition on entropy generation.

3. Using the maximum allowable entropy generation per unit mass as a criteria in defining life span. As long as the organism performs its life functions, entropy continues to be generated. If we calculate the maximum lifespan entropy, then we can study the effect of the different factors on the time needed to reach lifespan entropy.

<u>The objective is to accurately calculate lifespan maximum entropy and predict the life span using the $\sigma_{m,max}$ concept, then compare with empirical data available for the BS.</u>

3.1 Hypothesis:

The Second law of thermodynamics dictates that a closed adiabatic system initially in a state of non-equilibrium tends towards equilibrium with increasing entropy. The difference between final entropy and initial entropy of such a system is called entropy generation. Living BS are open systems that are not in thermal, chemical or mechanical equilibrium with the environment. In order to keep these non-equilibrium conditions, there are intensive constant biological reactions inside the BS requiring exchange of energy and matter with the environment, thus, generating entropy. Internal equilibrium within BS and external equilibrium of BS with the surrounding usually means death.

If a CV is drawn around the BS, total entropy generated can be determined just by using entropy balance equation which accounts for fluxes (in/out) and entropy transfer due to heat fluxes. An alternative method would be to consider that all the activities performed by the BS require energy produced by its metabolism; therefore the analysis of entropy generated trough metabolic reactions should give a good approximation of entropy generated **<u>within</u>** the BS. This is the approach taken in the current paper, in which the estimated (daily) energy requirements (EER) of the BS were used to calculate the metabolic rates, and then an availability analysis was applied to the metabolic reactions of the main nutrient groups to obtain the entropy generated. The hypothesis presumes that nutrients not metabolized leave the BS without significant change in their entropy, and that differences between the entropy inflow/outflow of water and air are small; such an assumption is supported by the work of Hershey and Wang in which the entropy exchange due to breathing (considering the change in both temperature and chemical composition of breathing air) was less than 2.5% of the total entropy generated by the human body..

4. Analysis

A phenomenological analysis will be presented first followed by more rigorous analyses.

4.1 Phenomenological Analysis

If a resting person of about 70 kg is losing energy (called heat loss) at the rate of 70 W ($\dot{Q}$), then the person can maintain a body temperature of 37 C (T) if the body generates energy at the rate of 70 W. Consider a BS of body mass m, volume V and surface area A. The rate of heat loss is proportional to the difference in temperature between the body surface and the temperature of the surroundings (T_0). Assuming the surface temperature is the same as T, the minimum specific metabolic rate ($\dot{q}_m$) required to overcome heat loss is given as [6]:

$$\dot{q}_m(kW/kg) = \dot{Q}/m = h_H A(T-T_0)/m \tag{3}$$

Where h_H, the heat transfer coefficient in kW/m^2 K and $\dot{Q}$, heat loss rate in kW. If the body surface area of BS, $A \propto R^2_{Char}$ where R_{char} is the characteristic size of BS and mass of BS, $m \propto R_{Char}^3$, then $A \propto m^{2/3}$ (empirical relation $A \propto m^{0.664}$)

$$A/m \propto 1/R_{Char} \propto 1/m^{1/3} \tag{4}$$

$$\dot{q}_m \propto 1/m^{1/3} \rightarrow \dot{q}_m = C_m m^{-1/3} \tag{5}$$

where C_m is constant. The empirical fit of experimental data indicates:

$$\dot{q}_m = C_m m^{-0.26} \tag{6}$$

where $C_m = 3.552$ ($W/kg^{0.74}$) and $\dot{q}_m$ is given in (W/kg). While simple theory predicts the exponent to be -0.333, empirical experimental fit yields the exponent to be -0.26. If ATP production is accounted for, the heat production rate must be more than the value given by Eq. (6).

Integrating eq. (5) over life time (t_{life}) with the same specific metabolic rate:

$$\dot{q} t_{life} = q_{m,life} (kJ) = C_m t_{life} m^{-1/3} \tag{7}$$

Assuming a life span of 75 years, constant metabolic rate, and a 65 kg individual, q_{life}=2,840 MJ/kg. This is clearly an overestimate since specific metabolic rate keeps decreasing with increase in the mass. If Rubner's hypothesis of specified $q_{m,life}$ (J/kg) is correct, then Eq. (7) yields:

$$t_{life} \propto m^{1/3} \tag{8}$$

If one adopts the second law approach of entropy generation concept and ignores the entropy exchange through convection compared to the entropy through transfer of metabolic heat ($\dot{Q}$), the entropy (S) balance equation for a closed system yields

$$dS/dt = \dot{Q}/T + \dot{\sigma} \tag{9}$$

where T_b is the body temperature. If BS is maintained at constant m, T and P, a first approximation yields dS/dt =0; thus,

$$\dot{\sigma} = -\dot{Q}/T \tag{10}$$

where $\dot{Q} < 0$. If one ignores ATP production, specific entropy generation rate ($\dot{\sigma}_m$) is given as:

$$\dot{\sigma}_m = \dot{Q}/(m\, T_b) = -\dot{q}_m/T = C_m m^{-n}/T \tag{11}$$

With Sparkman's data on the average lifetime energy of 3,025 MJ/kg and $T_b = 310$ K , Eq.(11) yields the lifetime entropy generated as 9753 kJ/kg K. Integrating with life span, it is apparent that:

$$\dot{\sigma}_m t_{life} = -\dot{q} t_{life} / T = C_m t_{life} m^{-n} / T \tag{12}$$

$$t_{life} \propto m^n \tag{12b}$$

where n~1/3, with experiments yielding n~0.2. Thus, constant energy expenditure also implies constant entropy generation over a life span when ATP production is not considered.

If one wishes to account for overall metabolic efficiency η and assume it to be the same for all nutrients throughout a life span, then $\dot{Q}$ is approximately given as $\dot{Q}(1-\eta)$, the scaling law given by Eq. (12b) is still valid except the life span will be increased due to reduced $\dot{Q}(1-\eta)$. It is seen that the higher the ATP conversion, the lesser the thermal dissipation; however, the thermal dissipation is still a necessary part of metabolism for warm blooded invertebrate in order to overcome heat losses.

4.2 Rigorous Analysis

a) Overview on present methodology

The phenomenological analysis does not consider the effect of variation in entropy generation with nutrient intake or age. To estimate entropy generation $\dot{\sigma}_m$ during a human life span, an availability analysis is applied to the metabolic oxidation of the 3 main nutrient groups: carbohydrates (CH), fats (F), and proteins (P), in order to obtain the entropy generated for each of them under isothermal conditions. Then databases from the Food and Nutrition Board (FNB) and the Center for Disease Control and Prevention (CDC) are used to obtain the estimated real energy requirement for a typical individual (as opposed to BMR), and this energy is converted to amounts of CH, F and P required using the nutrient heating values and the recommended diet composition (% of CH, F and P) found in medical literature. Once the quantity and distribution of food is known, the results from the isothermal availability analysis can be used to obtain the $\dot{\sigma}_m(t)$ due to metabolism. The total entropy generated over a life span is then computed.

Once the lifetime entropy generation is determined, the concept is used to predict changes in life span by modification on the initial assumptions; specifically, the effect of different physical activity levels is studied. Finally, some insights on future research are addressed.

b) Assumptions

- The essential nutrients are Carbohydrates (CH), fats (F) and proteins (P).
- CH, F and P will be modeled using glucose, palmitic acid, and average amino acids composition respectively.
- The time span of interest is much longer compared to metabolic reaction time scales; thus, quasi-steady approach is valid.
- The MWE for conversion of CH, F and P energy into ATP is different for every nutrient but remains constant over the whole life span. Thus, a child who is physically active requires more metabolic rate to produce necessary ATP rather than increased MWE.
- Metabolic rate and MWE are the same throughout the body including all body organs. It is known that oxidation near heart cells require more ATP, requiring increased MWE or increased metabolic rate.
- Actual energy requirements are used instead of basal metabolism in order to include the entropy generated by physical activity.

- ○ Functioning normally, human beings and other large organisms cannot tolerate changes of body temperature of more than a few degrees[16], and can be considered isothermal. One may assume that biochemical reactions in humans proceed at constant temperatures and pressures.

- ○ It is presumed that entropy generated for the metabolic part of the body determines the life span of BS since they produce ATP which enables the body to perform life sustaining functions and the metabolic mass of the body is proportional to body total mass.

- ○ The nutrient consumption data are based on normal gravity environment.

- ○ It will be assumed that a low-active physical activity level is the best representation of the healthy average individual activity.

- ○ In order to keep the physics simple, we assume all of ATP is converted into work and there is no dissipative heat produced by ATP.

- ○ All the processes within BS occur isothermally.

- ○ For warm blood invertebrate, only 10% of the feed is converted into body substance called efficiency of conversion of ingested food (ECI). Note that for cold blooded vertebrate the ECI could be as high as 44 % (e.g. German Cockroaches). Thus the analysis is essentially for warm blooded vertebrate only; hence it is assumed that the feed ration is essentially used for conversion to ATP and dissipative heat.

Calculations will be made on the average healthy male and female individuals of the U.S. population in the 50th percentile height and weight.

4.3 Governing Equations

a) Energy Conservation:

The First Law is a statement of energy conservation, and can be expressed for any system as [6]:

$$\frac{dE_{cv}}{dt} = \dot{Q}_{cv} - \dot{W}_{cv} + \sum_k \{\dot{m}_k e_{T,k}\}_i - \sum_k \{\dot{m}_k e_{T,k}\}_e$$

(13)

The total enthalpy ($e_{T,k}$, kJ/kg of k) includes the sum of internal energy (u in kJ/kg), flow work to cross the boundaries, and kinetic and potential energies of the advection terms for each species k. The term E (in kJ) includes internal (U in kJ), kinetic, potential, and chemical energies, among others.

b) Availability Balance:

When availability analysis is used, the compliance of both first and second laws of thermodynamics is ensured. The availability analysis yields:

$$\frac{d\{E_{cv} - T_o S_{cv}\}}{dt} = \dot{Q}_R \left[1 - \frac{T_0}{T_R}\right] + \sum_k (\dot{m}_k \psi_k)_i - \sum_k (\dot{m}_k \psi_k)_e - \dot{W}_{cv} - T_o \dot{\sigma}_{cv}$$

(14)

Where the flow or stream availability (ψ, work potential of energy, kJ/kg) at the inlet or exit are defined as

$$\psi_k(T, P, X_k, T_0) = [h(T,P) + ke + pe]_k - T_0 s_k(T,P)$$,

(15)

$\dot{m}_k$, mass flow rate of component k (kg/s), T_0 is the temperature of the surroundings with which the system exchanges heat, T is the temperature of nutrient and air intake (T= T_i) and exhaust (T= T_e),

$\dot{W}_{CV}$ represents all forms of work including PdV work of deforming CV (e.g. human body during growth; expansion of lungs during breathing in and out). The subscripts ($_{CV}$) and ($_R$) in Eq. (14) correspond to the control volume and thermal reservoirs respectively. For any ideal gas component k, the specific entropy (s_k) of component k is given as

$$s_k, \frac{kJ}{kg\ K} = s_k^{\ 0}(T) - R_k\ \ln\frac{p_k}{P^\circ}, \tag{16}$$

$$p_k = X_k * P, \quad R_k = \frac{\overline{R}}{M_k} \tag{17}$$

Where $\dot{m}_k$, X_k is the mole fraction of the component k, p_k, partial pressure of component k in bars, R_k is gas constant of species k {kJ/(kg K)} and $\overline{R}$ is universal gas constant {8.314 kJ/(kmole K)}. The p_{ref} is typically 1 bar. A statement of Eq. (14) is that the availability accumulation rate of any system is equal to the availability input due to heat transfer from external thermal reservoirs (e.g. radiant heaters used near incubators), less the availability transfer through work, and change due to advection and availability loss through irreversibility (=To $\dot{\sigma}_{cv}$). The entropy generation within selected CV is due to internal irreversibility caused by chemical reactions within all the reacting cells of BS, external irreversibility due to temperature gradient near the skin and irreversibility due to inhaled air being at T_0, which is different compared to T. When temperature T_0 is set equal to T, body temperature of BS (e.g. CV boundary just below skin), then the irreversibility estimation or entropy generation rate $\dot{\sigma}_{cv}$ is due to all irreversible processes occurring within the BS.

4.4 Simplifications

a) Gibbs free energy and Isothermal Chemical Reactions:

If CV is selected such that the boundary temperature T_0 in Eq. (14) is set as body temperature T and neglecting kinetic and potential energies and external heat inputs, then the stream availability in Eq. (15) is equal to the Gibbs free energy and Eq. (14) becomes

$$\frac{d\{U_{cv} - T_o\ S_{cv}\}}{dt} = \sum_k \left(\dot{m}_k\ g_k\right)_i - \sum_k \left(\dot{m}_k\ g_k\right)_e - \dot{W}_{cv} - T_o\dot{\sigma}_{cv} \tag{18}$$

where

$$\psi_k(T,P,X_k) = h_k(T,P) - Ts_k(T,P,X_k) \approx g_k(T,P,X_k) \tag{19}$$

The Gibbs function g of any chemical constituent k is defined as $g_k = h_k - T\ s_k$ where h_k is enthalpy and s_k is entropy of the constituent; the lower is h_k and the higher is s_k, lower is "g_k". Like temperature T, pressure P, and enthalpy h, the "s" and g are also properties and value for any given pure component k, the s and g are fixed once T and P are specified. Eq. (18) is equally applicable to each organ of BS across which reactants enter and products leave. Adding over all metabolic cells within the body, the $\dot{m}_k$ represents total mass of nutrient species k entering the body. Macro-nutrients (reactants) are constantly injected at T, the required oxygen is supplied with air inhaled at T, and products exhausted through exhaling at T.

Simplifying the left-hand side of Eq. (18), the availability accumulation due to body growth is give as,

$$\frac{d(U_{CV}-TS_{CV})}{dt} = m\frac{d(u_{CV}-Ts_{CV})}{dt} + (u_{CV}-Ts_{CV})\frac{dm}{dt} \approx (u_{CV}-Ts_{CV})\frac{dm}{dt} \qquad (20)$$

For any given reaction "j" the change in Gibbs's free energy per unit mass of metabolized component j (kJ/kg of j) is given as:

$$\Delta G_j = G_{P,j} - G_{R,j} = \Delta G_j(T,P) + R\,T\,\ln\frac{X_{P1}\,X_{P2}}{X_{R1}\,X_{R2}} \qquad (21)$$

where mixture is assumed to be an ideal mixture. The first term on the right is much larger than the second term. Equation (21) shows free energy dependency on temperature, pressure and concentration, ΔG^o is the free energy in standard conditions as used in biochemistry, and $[X_{p1}]$ and $[X_{R1}]$ stands for products and reactants molar fractions.

$$\Delta G_j(T,P) = G_{P,j} - G_{R,j} \approx \Delta G_j^{\circ}(T) \qquad (22)$$

Where $\Delta G_j^{\circ}(T)$ is at a pressure of 1atm. It will be shown later that the change in free energy will allow us to find an approximate value of entropy generation during isothermal chemical reactions for selected macro-nutrients, such as those occurring in biological systems. Three chemical reactions for CH, F and P are considered. Using Eq. (22) in Eq. (18) and assuming steady state {i.e neglecting the unsteady term given by Eq.(20) },

$$\dot{W}_{cv,j} - \dot{m}_j\left\{G_{R,j} - G_{P,j}\right\} + T\,\dot{\sigma}_j = 0\,, \quad j = CH\,, F\,, P \qquad (23)$$

b) Metabolism, Work in Biological Systems and Bioenergetics:

The BS converts the chemical energy of food (i.e. three basic groups of macro-nutrients: CH, F and P) into thermal and mechanical energy (work through ATP production) using the cellular respiration process.. Let us first consider the pure oxidation of glucose (j = CH).

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O \qquad (24a)$$

$$\Delta\bar{G}_c^{\,o} = G_P - G_R = -2.87 \times 10^6 \text{ kJ/kmol or } \Delta G_C^o = 15929 \text{ kJ/kg glucose}$$

where ΔG_c^o is Gibb's free energy for a conventional combustion process. The macro-nutrients contain chemical energy at low entropy level (high G_R) while the products (CO2 and H2O) have high entropy (low G_P) due to release of thermal energy. Hence typically $\Delta G_c^o < 0$. Now consider the metabolic oxidation of glucose along with ATP production, which can be expressed as:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + 36 \text{ ATP} \qquad (24b)$$

$$\Delta\bar{G}_M^{\,o} = -1.79 \times 10^6 \text{ kJ/kmol or } \Delta G_M^o = 9935 \text{ kJ/kg glucose}$$

where ΔG_M^o is the Gibb's free energy change for a metabolic reaction. Then the work potential of ATP for running the BS is:

$$W_{max} = \Delta\bar{G}^{\,o}_{ATP} = \Delta G_M^o - \Delta G_C^o = 1.08 \times 10^6 \text{ kJ/kmol or } \Delta G^0_{ATP} = 5994 \text{ kJ/kg glucose}$$

Considering oxidation of component j, the metabolic efficiency (known as availability efficiency in thermodynamics literature) is defined as

$$\eta_j = \frac{\dot{W}_{cv,j}}{\dot{W}_{cv,opt,j}} = \frac{\Delta G^{\circ}_{ATP,j}}{\Delta G^{\circ}_{c,j}} \qquad (25)$$

Part of the available energy has been converted into chemical energy within the ATP molecules. The efficiency is about 38% while 62% is wasted as heat for CH. Table 1 shows properties for CH, F and P. Using Eq. (25) in Eq. (13) and under quasi-stead state, the heat transfer rate is given as

$$\dot{Q}_{cv} = \sum_j \left[1 - \eta_j\right]\left[\left(\dot{m}_j H_j\right)_P - \left(\dot{m}_j H_j\right)_R\right] + T\sum_j \eta_j \left[\left(\dot{m}_j S_j\right)_P - \left(\dot{m}_j S_j\right)_R\right]$$

Where $H_{j,P}$, enthalpy of products per kg of j and $S_{j,P}$, entropy of products per kg of j . As $\eta_j \to 0$ for j = CH, F, and P, all the chemical energy is converted into dissipative heat.

For proteins, weighted averages of a combination of 20 amino acids were used to obtain a normalized surrogated amino acid formula $C_{4.57}H_{9.03}N_{1.27}O_{2.25}S_{0.046}$ with an empirical molecular weight of 119.39 kg/kmol and a heating value of -385 MJ/kmol (5.5 kcal/g) calculated by the Boie equation which is widely used in combustion literature [6,7]. It is interesting to note that efficiency of protein metabolism is about 1/3 of the efficiency for carbohydrates and fats. This may explain why energy is obtained from proteins in very small quantities and usually when other sources of energy are not available. Thus, bodily functions of a system BS with protein intake must be highly impaired compared to BS consuming glucose. Cells being made mostly of protein molecules may get consumed in the event other sources of energy intake are not available leading to cell death and impairing body functions.

4.5 Entropy Generation

Consider any reaction j; Eq (25) yields

$$\dot{W}_{cv,j} = -\eta_j \dot{m}_j \Delta G°_{c,j} = -\dot{N}_j \Delta \overline{G}°_{c,j} , \quad \Delta G_{c,j} < 0, \quad j = CH, F, P \tag{26a}$$

where $\dot{N}_j = (\dot{m}_j / M_j)$, j = CH, F and P, N_j is the kmoles of j reacted per unit time (kmole/s), M_j, molecular weight of j and $\Delta \overline{G}_{c,j}$ change in Gibbs function per kmole (kJ/kmole of j). Summing up over the three reactions involving CH, F and P,

$$\dot{W}cv = -\sum_j \eta_j \dot{m}_j \Delta G°_{c,j} = -\sum_j \eta_j \dot{N}_j \Delta \overline{G}°_{c,j} , \quad j = CH, F, P \tag{26b}$$

Then using Eq. (26b) in Eq.(23) for $\dot{W}_{cv}$ and simplifying

$$\dot{\sigma}(t) = \frac{\sum_j (1 - \eta_j)\dot{m}_j(t) \left(-\Delta G°_{c,j}\right)}{T} = \frac{\sum_j (1 - \eta_j)\dot{N}_j(t) \left(-\Delta \overline{G}°_{c,j}\right)}{T} , \quad j = CH, F, P , \Delta G_{c,j} < 0 \tag{27}$$

Typically $\Delta G°_{c,j} = \Delta H°_{c,j} - T\Delta S°_{c,j} \approx \Delta H°_{c,j}$. Thus $\dot{m}_j(t) \Delta G°_{c,j}(T, P) \approx \dot{m}_j(t) \Delta H°_{c,j}$, metabolic rate [see Ref 6]. Thus the numerator in Eq (27) could be approximately interpreted as wasted heat for the whole BS. Eq. (27) can be equally extended to individual organs (heart, liver, kidney etc) if system is elected around each organ and $\dot{\sigma}$, η_j and { $\dot{m}_j(t) \Delta H°_{c,j}$ } are interpreted as entropy generation rate, metabolic efficiency and metabolic rate of the organ.

If η_j is low (e.g. proteins), then $\dot{\sigma}(t)$ is higher. Note that $\dot{\sigma}$ reaches a maximum when $\eta \to 0$ (all energy is dissipated as heat) and $\dot{\sigma} \to 0$ as $\eta \to 1$. The latter result is due to the assumption that ATP simply serves as the "work" equivalent in thermodynamics. However, as ATP is used for pumping blood, the pressure loss through blood vessels is converted into heat. Also it is known that about 75% of energy released from ATP in muscles goes to mechanical work of a contraction, while 25% is released as heat. Thus, an equivalent metabolic efficiency (typically lower than true values) could be

used to account for conversion of a part of ATP into heat. The specific entropy generation per unit mass of the BS with time (aging) is given as:

$$\dot{\sigma}_m(t) = \frac{\dot{\sigma}(t)}{m(t)} \quad , \quad \text{kJ/(kg-s-K)} \tag{28}$$

where entropy generation rate and mass of BS keeps varying with time. The life span integrated value is obtained using:

$$\sigma_m(t) = \int_0^t \dot{\sigma}_m(t)\, dt \quad , \quad \text{kJ/(kg-K)} \tag{29}$$

5. Input data and procedure

5.1 Fuel Data

The properties of CH, F and P and free energy data are presented in Table 1. It is noted that the heat released per unit mass of stoichiometric oxygen is approximately constant for all three components with an average of 14,335 kJ/kg of O_2. Based on the above numbers and using 14,335 kJ/kg of O2 (or 18.7 kJ/L of O2), the ROL theory suggests that the lifetime oxygen consumed is 41.2- 77.4 kg of O_2/kg body mass (31,510-59,280 liter/kg body mass, without man) and 211 kg of O_2/kg body mass (161,560 liter/kg body mass) including man. With Rubner's data of 836 MJ/kg, the O2 consumption is 58.3 kg of O_2 /kg body mass (44,650 Liters/kg). Compare this with the metabolic potential (total O_2 consumed during lifespan per kg bodyweight) for a 2 g shrew or a 100,000 kg blue whale is approximately 38,000 L of O_2 consumed or 8.5 kmol ATP/kg body mass per lifetime [20].

5.2 Statistical Databases

The mole flow of macronutrients can be obtained from the estimated energy requirements (EER), correlations and AMDR/AI of the Dietary Reference Intake publication. The energy required for bodily functions and physical activity has been summarized and tabulated by the Food and Nutrition Board (FNB) for humans from birth to adulthood. The *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)* [28] revised and published by FNB in 2002, contains the most updated nutrition information for the US population. The values form this study, known as Dietary Reference Intake (DRI), are intended to serve as a guideline for nutrition.

Equations for energy requirements as a function of PAL age, weight and stature were presented in the DRI publication, as well as the recommended macronutrient distribution of food. The PAL levels are summarized in Table 2 while EER relations and values used in this study are presented in Table 3. The terminology for BMR, TEE, PAL and EER are explained in Appendix A.

One important note about the DRI study is that EER values were measured using the double-labeled-water technique and therefore they correspond to *field* metabolic rates. This technique is much more accurate than short-time laboratory measurements (calorimetry) or scaling-law correlations.

Table 1. Properties of Nutrients [27, 30].

Substance	Formulae	M	HHV kJ/kg	HHV$_{O2}$ kJ/kg O$_2$	h_f MJ/kmol	s_{298} kJ/kmol	Work conv. efficiency %
Glucose	$C_6H_{12}O_6$	180	15630	14665	-1260	212.0	38.2
Protein	$C_{4.57}H_{9.03}N_{1.27}O_{2.25}S_{0.046}$	119	22790	14705	-385		10.4
Fat	$C_{16}H_{32}O_2$	256	39125	13635	-835	452.4	32.2

Table 2. PAL walking equivalences [28].

PAL walking equivalences		Walking equivalence
PAL category	PAL value	(m/d at 2-4 mph) (*)
Sedentary	1.0 – 1.39	
Low Active	1.4 – 1.59	1.5, 2.2, 2.9 for PAL=1.5
Active	1.6 – 1.89	3.0, 4.4, 5.8 for PAL=1.6
		5.3, 7.3, 9.9 for PAL=1.75
Very Active	1.9 – 2.5	7.5, 10.3, 14.0 for PAL=1.9
		12.3, 16.7, 22.5 for PAL=2.2
		17.0, 23.0, 31.0 for PAL=2.5

(*) for relative heavy weight (120 kg), mid weight (70 kg) and light weight (44 kg) individuals

5.3 Adequate Macronutrients Distribution Range (AMDR) / Adequate Intake (AI)

ADMR and AI indicate the recommended % distribution or intake of each macronutrient group, as well as vitamins and minerals. The database includes AMDR for subgroups like saturated and polyunsaturated fatty acids (sub group of fats). Partial data is shown in Table 4.

5.4 Calculation Procedure

The last step is to perform numerical integration in order to obtain the life span using the concept of entropy generation. The procedure used for numerical integration is as follows:

- o Use of 0.25-year increments (trimesters, 91.5 days) within the age range from 0 to 90 years.
- o Use of growth data from CDC to obtain body size and weight as function of age for both genders and 50th percentile.
- o Use of age, stature and weight to estimate EER for different PAL's (Table 2) using DRI relations (Table 3).
- o Estimate food mass intake by a macronutrient group, using the EER values, distribution range from AMDR/AI (Table 4) and the heating value of each macronutrient (Table 1).
- o Apply Eq. (27) to obtain entropy generated.

- o Generate tables and charts for entropy generation per trimester and calculate cumulative entropy generated.
- o Express all data as per unit total body mass.
- o Though calculations are made for different activity levels, it is assumed that the Low Active (LA) PAL represents the best average of the healthy individual.

The case for the 50th percentile (height and weight) population, low active physical activity level (LA PAL) and the average value of the recommended AMDR/AI range is considered the base case. The average lifespan for the U.S. population is obtained from the CIA World Fact Book [29], and is found to be 74.63 years for males and 80.36 years for females (2004).

Table 3. EER (kcal/day) Correlation for average male individuals [28].

EER for Infants and Young Children, EER = TEE + Energy Deposition
0-3 months   (89 x weight of infant[kg] -100) + 175
4-6 months   (89 x weight of infant[kg] -100) + 56
7-12 months   (89 x weight of infant[kg] -100) + 22
13-35 months (89 x weight of child[kg] -100) + 20

EER for Boys 3 through 8 years, EER = TEE + Energy Deposition
EER = 88.5 - 61.9 x Age[y] + PA x (26.7 x Weight[kg] + 903 x Height[m]) + 20
Where PA is the physical activity coefficient:
PA = 1.00 if PAL is estimated to be > 1.0 < 1.4 (Sedentary)
PA = 1.13 if PAL is estimated to be > 1.4 < 1.6 (Low Active)
PA = 1.26 if PAL is estimated to be > 1.6 < 1.9 (Active)
PA = 1.42 if PAL is estimated to be > 1.9 < 2.5 (Very Active)

EER for Boys 9 through 18 Years, EER = TEE + Energy Deposition
EER = 88.5 - 61.9 x Age[y] + PA x (26.7 x Weight[kg] + 903 x Height[m]) + 25
Where PA is the physical activity coefficient, equal to the 3-8 years range.

EER for Total Energy Expenditure (TEE) for Men 19 years and older
EER = 662 - 9.53 x Age [y] + PA x (15.91 x Weight [kg] + 539.6 x Height [m])
Where PA is the physical activity coefficient:
PA = 1.00 if PAL is estimated to be > 1.0 < 1.4 (Sedentary)
PA = 1.11 if PAL is estimated to be > 1.4 < 1.6 (Low Active)
PA = 1.25 if PAL is estimated to be > 1.6 < 1.9 (Active)
PA = 1.48 if PAL is estimated to be > 1.9 < 2.5 (Very Active)

Table 4. AMDR/AI Data [28].

| Years	Carbohydrates		Total Fats		Protein	
	RDA/AI (g/d)	AMDR (%)	RDA/AI (g/d)	AMDR (%)	RDA/AI (g/d)	AMDR (%)
Infants						
0 0.5	60		31		9.1	
0.5 1	95		30		13.5	
Children						
1 3	130	45-65		30-40	13	5-20
4 8	130	45-65		25-35	19	10-30
Male						
9 13	130	45-65		25-35	34	10-30
14 18	130	45-65		25-35	52	10-30
19 30	130	45-65		20-35	56	10-35
31 50	130	45-65		20-35	56	10-35
50 70	130	45-65		20-35	56	10-35
>70	130	45-65		20-35	56	10-35
Female						
9 13	130	45-65		25-35	34	10-30
14 18	130	45-65		25-35	46	10-30
19 30	130	45-65		20-35	46	10-35
31 50	130	45-65		20-35	46	10-35
50 70	130	45-65		20-35	46	10-35
>70	130	45-65		20-35	46	10-35
Pregnancy						
≤18	175	45-65		20-35	71	10-35
19 30	175	45-65		20-35	71	10-35
31 50		45-65		20-35	71	10-35
Lactation						
≤18	210	45-65		20-35	71	10-35
19 30	210	45-65		20-35	71	10-35
31 50	210	45-65		20-35	71	10-35

6. Results

6.1 Base case

Figures 1 and 2 present the entropy generation rate and cumulative value for the base case. Table 5 presents the base case data for the male and female individual in the 50th percentile (weight and height) and low active PAL.

Figure 1. Entropy generation rate for the base case.

Entropy Generation Rate per body mass, Low Active PAL
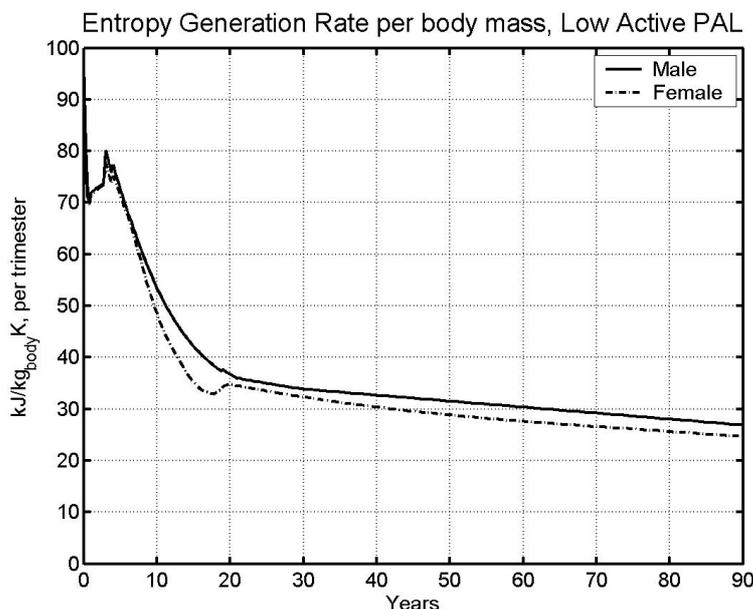
Figure 2. Cumulative Entropy generation for the base case.

Cummulative Entropy Generation per body mass, Low Active PAL
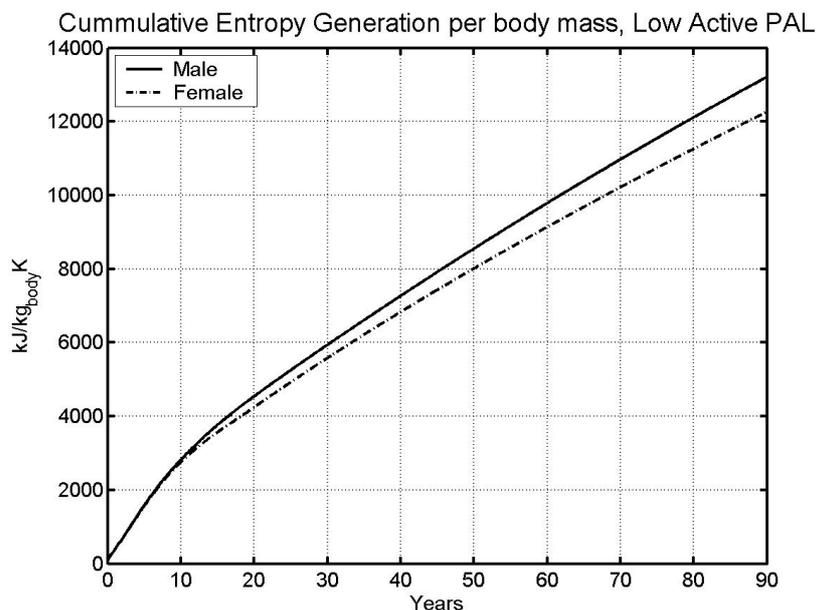
It can be seen that the specific entropy generation rate is always positive and the rate declines up to 18 years age, then it declines at a less steep rate during the whole lifespan. Specific entropy generation rate reduces with age: the generation rate at 75 years is 1/3 of that of the 1-year-old baby. It is noted that the rate for a baby is high since specific metabolic rates (the reason kids being active with higher rate of production of ATP per unit mass) are high due to large surface area to volume ratio for smaller sized BS [6,7]. A 3.5-kg newborn is expected to consume oxygen at a rate of 27 cm^3/min which corresponds to a heat release rate of 8.4 W (or 2.4 W/kg body mass) [32] which is higher compared to an adult (≈ 0.8 W/kg).

Table 5. Entropy generation base case data, 50th percentile population.

	Male	Female
Av. Lifespan [5]	74.63	80.36
Entropy generated (kJ/kg-K)	11 508	11 299

Cumulative values of entropy generated (figure 2) show a steady increase over the human lifespan, with a higher rate during the first years. It is seen that $\dot{\sigma}_m$ is higher near birth due to low body mass. If one extrapolates $\dot{\sigma}_m$ to the time of conception, it may be infinite since m → 0. For males, $\sigma_{m,life}$ at 74.63 years age is 11,508 kJ/kg-K, while females at 80.36 years age have $\sigma_{m,life}$ of 11,299 kJ/-K. These values are close together (less than 2% difference), enforcing the idea of a fixed amount of entropy generation per unit body mass during a lifetime. We will assume $\sigma_{m,life}$ = 11,404 kJ/kg-K for subsequent parametric studies on a human lifespan.

One interesting fact about our calculation method is that it can be applied to any species if the growth charts, energy requirements and diet composition are known. Using the data from Romsos et al. [31] for growth and diet composition of dogs (female Beagles only) and the metabolic energy requirements from Payne [13] and Thonney [14], we estimated the average $\sigma_{m,life}$ for Beagle bitches to be 3,874 kJ/kg-K. We were expecting the lifetime specific entropy generation to be similar among species, but for a dog to reach the same level of entropy generation as a human would require a life span of 43 years, which is 3 times the average of 13.5 years typical of Beagles. However, some similarities with the human data were observed as puppies generate 3 times more entropy than adult dogs. More research in this area is necessary to fully understand how the concept translates between different biological species.

6.2 Effect of physical activity level

The procedure in which different PAL's are introduced in the base case is through a correction factor. The PAL factors used were presented in the EER correlations on table 3. The predicted lifespan to reach limit entropy is shown in Table 6, and the plots for male individuals are in Figures 3 and 4.

**Table 6.** Change in lifespan vs. physical activity level (PAL).

	Case	Lifespan to limit entropy(y)	
		Male	Female
S -	Sedentary	85.05	95.75
LA -	Low Active (base)	73.78	81.61
A -	Active	63.78	69.53
VA -	Very Active	53.20	57.68

The data above shows that physical activity effect on the life span required to reach limit entropy is very significant. It suggests that as PAL increases, life span is shortened, which somehow contradicts

medical literature that recommends a minimum level of PAL to maintain a good health and increase life span. However, neither concept has to be wrong: a minimum PAL is helpful to increase life span in order to maintain functional capability of body organs, but excess activity accelerates the body's wear and tear. It may be possible that an "optimum" exist so that entropy generation is minimized while health problems due to sedentary life style (accumulation of fats, for example) are avoided. For example, at sedentary level "fat" accumulates in the body, reducing the fraction of metabolic part of the body mass, which is not considered in the present analysis.

This reasoning leads to the definition of the Low Active physical activity level as the best compromise. In Figures 3 and 4, Low Active PAL is the solid dark line.

Figure 3. Entropy Generation rate for different physical activity levels.
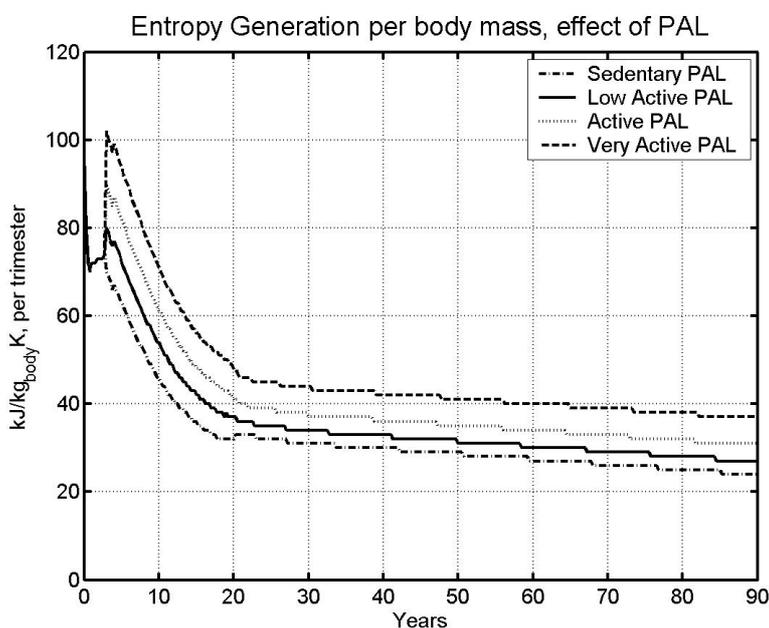
Figure 4. Cumulative Entropy Generation for different physical activity levels.
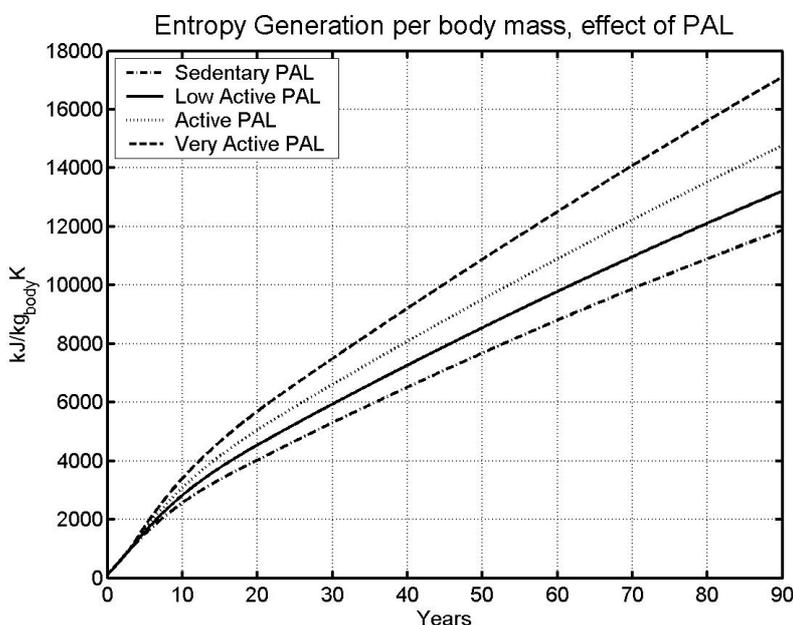
6.3 Gravitational Effects

In addition to assumption of nutrient data based on normal gravity environment, it is further assumed that, due to the absence of body weight, a zero gravity environment (space) is equivalent to a change of PAL from Low Active to Sedentary. A male astronaut between 25-35 years age who experiences a 3 month period of zero-gravity will increase his life span by 9.5 days, while in a woman the increase will be 11.5 days. This means around 40 days life span increase for every year spent in space. To increase the life span 1 year, a 25 years old male astronaut will have to live 9.5 years in space, while the female astronaut will require 7.5 years. However, the effect of growth must be accounted for. These long exposures to zero-gravity are not typical of today's space missions, but they may become true, for example, if attempts are made to send humans to Mars. These preceding predictions do not include any negative health effects (e.g. tissue growth and repair, ATP production, clog free blood vessels, etc) that can be caused by long term exposition to zero-gravity.

7. Conclusions

o The basic laws of thermodynamics were applied to biological systems, using a combination of laws of thermodynamics and available information from biochemistry literature and updated CDC databases. Entropy generated was determined for metabolism of the typical components of the human diet, and total entropy generation was estimated through numerical integration for the average population.

o Data on average lifespan was used to obtain lifetime limit entropy, which was found equal to 11,404 kJ/kg-K. This value of entropy predicts life span within 1.5% of the life span from literature (predicted: 73.78 and 81.61 years; Literature: 74.63 and 80.36 years; males and females respectively).

o Entropy generation rate was found to be 3 times higher on babies than on elderly, and in general, lifetime entropy curves showed similar trends and values to those of the previous work of Hershey and Wang [24, 25], though the values obtained in this work are approximately 5-10% higher.

o The higher the specific metabolic rate (kW/kg), the higher the specific entropy generation rate (kW/kg), and the faster we approach the specific entropy generation limit over a lifetime (kJ/kg K).

o The entropy generation rate depends upon the type of ration fed to BS.

o When a non-zero gravity environment is approximated as a change from low active to sedentary PAL, it is possible to predict changes on the lifespan of astronauts based on the exposition time to the weightless condition. It was found that a male astronaut will extend his life span 1 year for every 9.5 years he spent in space. For a female astronaut, this time was estimated as 7.5 years.

o The present approach presumes that the ATP acts as work currency, generating no entropy.

o While the present analysis for entropy generation is conducted considering the human as a whole system, the analysis can be extended to determine the entropy generation for each organ of the system (heart, kidney, liver etc) and to determine which degenerates rapidly as long as metabolic rates and metabolic efficiencies of the organ are known.

Appendix A - Terminology

Basal Metabolic Rate (BMR)

BMR is the rate of energy expenditure which occurs in the post-absorptive state, defined as the particular condition after an overnight fast, with the subject having not consumed food for 12 to 14 hours and resting comfortable, supine, awake and motionless in a thermo neutral environment. This metabolic state corresponds to the situation in which food and physical activity have minimal influences in metabolism. When extrapolated to 24 hrs, BMR is called Basal Energy Expenditure (BEE).

Total Energy Expenditure (TEE)

TEE is the sum of BMR, thermal effect of food, thermoregulation, physical activity and the energy expended in depositing new tissues (growth) and/or producing milk (lactation), though it doesn't account for the energy content of those tissue constituents or milk. This data was used to estimate the TEE.

Physical Activity Level (PAL)

PAL is the ratio of total to basal energy expenditure (TEE/BMR). It is divided in 4 main categories: Sedentary $(1 - 1.4)$, Low Active $(1.4 - 1.6)$, Active $(1.6 - 1.9)$ and Very Active $(1.9 - 2.5)$. Table 2 presents PAL categories and its equivalences.

Estimated Energy Requirements (EER)

EER is the TEE modified to account for the energy content of tissues and milk production (lactation), body composition, size, growth, age, gender and PAL, among others.

Databases

The Center for Disease Control and Prevention (CDC) maintains a database for growth in weight and stature as a function of age for the US population. The database contains values for ages from 0 to 20 years, both genders, and several percentiles. Those values were used in this study as input for the energy requirement correlations obtained from the DRI publication (see Table 4). Growth data for ages over 20 years was obtained from additional sources, as well as the % of body fat as a function of age and gender [33].

References

1. Olshansky, S.J.; Carnes B.A.; Butter R.N. If humans are built to last. *Scientific American* **2001**, *284*, 70-75.
2. Olshansky, S.J.; Carnes B.A. *Quest for Immortality: Science at Frontiers of Aging*; Nortons: New York, NY, 2001.
3. Olshansky, S.J.; Carnes, B.A.; Desequelles, A. Prospects for Human Longevity. *Science* **2001**, *291*, 1491-1492.
4. Goldstein, M.; Goldstein, I.F. *The Refrigerator and the Universe*; Harvard Press: Harvard, 1993.
5. (a) Rubner, M.Z. *Biology* **1883**, *19*, 535-562; (b) Pearl, R. *The Biology of Death*; J.B. Lippincott: Philadelphia, 1922.
6. Annamalai, K.; Puri, I. *Advanced Thermodynamics Engineering*; CRC Press: Boca Raton, FL, 2002.
7. Annamalai, K.; Sweeten, J.M.; Ramalingam, S. Estimation of Gross Heating Values of Biomass Fuels. *Transactions of the ASAE* **1987**, *30*, 1205-1208.
8. Craig, R.W.; Roger, S.S. Allometric scaling of mammalian metabolism. *J. Exp. Biol.* **2005**, *208*, 1611-1619.
9. (a) Hofman, M.A. Energy, Metabolism, Brain Size and Longevity in Mammals. *Quart. Rev. Biol.* **1983**, *58*, 495-512; (b) Hofman, M.A. Evolution of brain size in neonatal and adult placental mammals: a theoretical approach. *J. Theor. Biol.* **1983**, *105*, 317-332.
10. Schmidt-Nielsen, K.S. Why Is Animal Size So Important? Cambridge University Press: Cambridge, 1984.
11. West, G.B.; Brown, J.H.; Enquist, B.J. A General Model For The Origin Of Allometric Scaling Laws In Biology. *Science* **1997**, *276*, 122-126.
12. West, G.B.; Savage, V.M.; Gillooly, J.; Enquist, B.J.; Woodruff, W.H.; Brown, J.H. Response to Darveau *et al.*: Why Does Metabolic Rate Scale With Body Size? *Nature* **2003**, *421*, 713.
13. Payne, P.R. Assessment of the Protein Values of Diets in Relation to the Requirements of the Growing Dog. In *Canine and Feline Nutritional Requirements*; Graham-Jones, O., Ed.; Pergamon Press: London, 1965; pp. 19-31.
14. Thonney, M.L.; Touchberry, R.W.; Goodrich, R.D.; Meiske, J.C. Intraspecies Relationship Between Fasting Heat Production and Body Weight: A Reevaluation of W^{75}. *J. Anim. Sci.* **1976**, *43*, 690.
15. Subcommittee on Dog Nutrition, Committee on Animal Nutrition, Board on Agriculture, National Research Council. *Nutrient Requirements of Dogs* (Revised 1985); National Academy Press: Washington, D.C., 1985.
16. Demetrius, L. Caloric Restriction, Metabolic Rate, and Entropy. *J. Geront. Ser. A: Biol. Sci.* **2004**, *59A*, 902-915
17. Bejan, A. The Tree of Convective Heat Streams: Its Thermal Insulation Function and the Predicted 3/4-Power Relation Between Body Heat Loss and Body Size. *Int. J. Heat Mass Trans.* **2001**, *44*, 699-704.
18. Bejan, A. Constructal Theory: From Thermodynamics and Geometry Optimization to Predicting Shape in Nature. *Energy Conver. Mgmt.* **1998**, *39*, 1705-1718.

19. Bejan, A.; Lorente, S. The Contructal Law and the Thermodynamic of Flow Systems with Configuration. *Int. J. Heat Mass Trans.* **2004**, *47*, 3202-3214.

20. Dobson, G.P. *Clin. Exp. Pharmacol. Physiol.* **2003**, *30*, 590-597.

21. Azbel, M.Y. Universal Biological Scaling and Mortality. *Proc. Nat. Acad. Sci. USA* **1994**, *91*D, 453-457.

22. Spearman, J.R. Review Body Size, Energy Metabolism and Lifespan. *J. Exp. Biol.* **2005**, *208*, 1717-1730.

23. Vaanholt, L.M. The rate of living in mice: impacts of activity and temperature on energy metabolism and longevity. Ph.D. Thesis, University of Groningen. 20 Feb. 1979; available online: http://dissertations.ub.rug.nl/faculties/science/2007/l.m.vaanholt/

24. Hershey, D. *Lifespan and Factors Affecting it*; Charles C. Thomas Publisher: Springfield, 1974.

25. Hershey, D.; Wang, H. *A New Age-Scale for Humans*; Lexington Books, 1980.

26. Batato, M.; Deriaz, O.; Jequier, E.; Borel, L. Second Law Analysis of The Human Body. In *Proc. Florence World Energy Research Symposium*, Firenze, Italy, May 1990.

27. Silva Hernandez, C. Entropy Generation in the Human Body. Estimation by means of Energy Requirements; MSME Final Report, Texas A&M University, 2004.

28. Anon. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*; National Academy Press, 2002.

29. CIA World Fact Book (www.cia.gov).

30. Nelson, D.; Cox, M. *Lehninger Principles of Biochemistry*; Worth: New York, NY, 2003.

31. Romsos, D.R.; Belo, P.S.; Bennink, M.R.; Bergen, W.G.; Leveille, G.A. Effects Of Dietary Carbohydrate, Fat And Protein On Growth, Body Composition And Blood Metabolite Levels in The Dog. *J. Nutr.* **1976**, *106*, 1452.

32. Mayhew, T.M. Allometric studies on growth and development of the human placenta: growth of tissue compartments and diffusive conductances in relation to placental volume and fetal mass. *J. Anat.* **2006**, *208* , 785–794.

33. Forbes, G. *Human Body Composition, Growth, Aging, Nutrition and Activity*; Springer-Verlag: New York, NY, 1987.