





Research Article

Thermodynamic Assessment of the Impact of Pregnancy and Lactation on the Longevity of Women

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Abstract

Effects of the pregnancy and the following lactation periods on the lifespan entropy of the women has been evaluated. In the case of singleton pregnancy, a wealthy woman may generate 1.5% and in the case of twin pregnancy 2.1% of the total lifespan entropy of a non-pregnant wealthy women. In the case of a poor woman the singleton pregnancy, may generate 1.8% and in case of the twin pregnancy 2.1% of the total lifespan entropy generated by the non-pregnant wealthy woman. Results of the diet-based thermodynamic calculations for the poor women are compared with the demographic data collected across pre-industrial Europe and a good agreement was found.

Keywords: *Thermodynamic assessment; entropy generation; diet-based entropic age; telomere length-based energy efficiency; pregnancy; lactation; historic demographic data.*

1. Introduction

The ageing research is carried in different paths: morphological cellular changes are traced with highly advanced observation techniques [1,2]. Joseph et al, [3] argued that the chemical reactions of cellular energy metabolism produce reactive oxygen species as byproducts; the oxidative damage accelerates aging via damaging the DNA, proteins and lipids. Mechanisms of occurrence of the ageing related distortion of the DNA strands and the struggle of the cells to counter this constitute another major ageing research path [4-10]. Although the organisms have a defense mechanism against the oxidative damage, it can still occur, especially if the organisms are not taking in adequate antioxidants from their diets. Accumulation of oxidative damage in the tissues accelerates aging [11, 12]. Living organisms are far from equilibrium structures, and they have a great tendency for approaching the equilibrium, which implies aging and increased entropy [13]. To survive at far from equilibrium, a living being should develop an entropy gradient with their surroundings. Such gradients are maintained only by utilizing energy imported from outside, so an open system may move away from near towards far from equilibrium. One of the major paths of the ageing research employs the fundamental principles of the thermodynamics and refers to the “entropic age” concept to study the ageing associated overwhelming of the maintenance systems of the body and the loss of molecular functions [14-16]. Silva and Annamalai [17, 18] and Annamalai, and Silva [19] quantified the entropy generation related ageing stress on individual organs. Living organisms maintain a highly organized structure by exporting entropy [20]. A fraction of the generated entropy accumulates in the

body increases disorder and structural impairment [13]. All the living beings die after reaching the lifespan entropy generation limit, since their bodies cannot stand accumulating more damage. Genetically induced repair and replacement processes are capable of maintaining the balance in favor of the functioning molecules when the organisms are young, but with ageing the balance between these processes tends toward inactivation and malfunctioning [14-16]. Following exactly the same behavior as the other dissipative systems, energy is needed to prevent entropy accumulation and heal the collected damage [21]. As explained by Yalcinkaya et al. [22] with the decline of the mitochondrial energy conversion, organisms start experiencing structural impairment. The concept of “entropic age” helps to quantify the damage accumulation by an organism in a systematic manner. The rate of living slowly wears out the cellular machinery, so a faster metabolism will “wear out” it more quickly. In their studies on thyroid function, Jumpertz et al [23], after following their subjects for 11 to 15 years, and deaths from natural causes concluded that for each 100-calorie (418 J) of additional nutrient uptake, corresponding to approximately $100 \times 100 / 1500 = 6\%$ additional intake, the risk of natural mortality increased by 25 to 29 percent. Caloric restriction and negative energy balance have been shown to reduce resting metabolic rate, and in contrast overeating increases resting metabolic rate [24,25]. Furthermore, caloric restriction has been consistently shown to extend maximal lifespan by up to 60 % in animals [26].

Kuddusi (2015) after noting that the people living in different regions of Turkey have different food habits calculated the lifetime entropy generation per unit mass of a

person and found substantial difference among their life expectancy. Kuddusi [27] determined that the metabolic entropy generation rate was 0.46×10^{-5} kW/kg K in the Marmara district of Turkey with the expected lifespan of 78.61 years, whereas in Eastern Turkey, metabolic entropy generation rate was 0.52×10^{-5} kW/kg K with the expected lifespan of 69.54 years. Patel and Rajput [28] performed similar calculations for different climate zones of India and Öngel et al [29] improved these analyses by incorporating the telomere effects. Entropic age concept suggests that a fast metabolism by generating more entropy could make people age more quickly.

1.1. Telomere Length as the Measure of the Thermodynamic Efficiency

Telomere length is birth-inherited and becomes about 50–100 base pair shorter every time the cell replicates [30]. At birth, there is no significant difference in telomere length between men and women. Telomere length remains higher in women than that of men as they age, probably because of their higher estrogen levels [31]. Estrogen has antioxidant properties that play a massive role in human reproduction and the menstrual cycle [32]. The disposable soma theory states that the organisms have limited resources to spend for their cellular processes; therefore, an investment for growth and reproduction will reduce the investment for DNA repair and open the way for cellular damage, shortened telomeres and accumulating mutations [33]. During energy deficiency, telomeres may interfere with signaling and re-direct critical resources to immediately important processes [34]; the longer telomeres may increase energy utilization efficiency [35]. An inappropriate pregnancy diet may lead to telomere shortening and chronic diseases [35]. Caloric restriction may change the energy allocation preference of the organisms. Roberts et al [36, 37] reported a significant effect of the food restriction to energy efficiency of milk production in baboon and rats. In the first trimester of pregnancy, estrogen and progesterone are secreted from the ovaries with stimulation of human chorionic-gonadotrophin originating from the placenta [38]. The circulating estrogen levels are elevated by approximately 100-folds in pregnancy and increase with gestational age [39]. The levels of sub-types of estrogen, i.e., estradiol, estrone, estriol, and estetrol, also increase [39]. During pregnancy, the estradiol levels are associated with consecutive pregnancies of the same woman [40]. Increased estradiol levels cause the plasma volume to increase and the up and downregulation of metabolizing enzymes and hepatic production of certain proteins. It improves binding of corticosteroids, sex steroids, thyroid hormones, and vitamin D to proteins [41, 42].

1.2. Effect of the Pregnancy and Lactation on the Longevity of Women

The effect of giving birth to babies and lactation on the longevity of women is ambiguous; there are conflicting observations in the literature, a negative relationship was reported by [43]. Smith et al [44], after employing the data available in the Utah Population Database regarding 13,987 couples married between 1860-1899 concluded that the women with fewer children as well as those bearing children late in life live had longer post-reproductive lives. Lycett et al [45] reported that the married women who did not give birth to babies did not live longer than the women who had babies and the women who had a few children did not live longer than the women who had many children, but reported

a trade-off between reproduction and longevity in the poorest social groups. Hsu et al [46] studied the fertility-longevity relationship by employing the data set of 81,924 women and 103,642 men born between 1601 and 1910 in Europe and concluded that higher fertility had a significantly negative effect on longevity and pointed the need for further research due to the multiple mechanisms of human ageing. Present study aims to contribute a thermodynamic opinion to this discussion.

2. Methods

2.1 Calculation of the Calories and the Macronutrients of Pregnancy and Breastfeeding Diets

Dietary Guidelines for Americans 2020-2025 [47] recommend the daily calorie intake range for healthy women aged 19 through 30 to be between 1,800 to 2,400 kcal/day. Trumbo et al [48] state that energy requirements in the first trimester would be the same as for non-pregnant women. During the second and third trimesters, energy needs increase by 340 cal/day (1,421 J/day) and 452 cal/day (1,889 J/day), respectively [49]. Kominiarek and Rajan [42] recommend carbohydrate intake should be 45-64% of the daily calories during pregnancy, and it should consist of 6-9 servings of whole-grain daily, and 20 to 35 % of the daily calories should be obtained from the healthy fats. The amount of protein intake should be increased by 25 g/day during the second and the third trimesters [48] and the breastfeeding period. Elango and Ball (2016) recommended the average daily protein intake for early and late pregnancy as 79 and 108 g/day, representing between 14-18% of the daily calories. Energy requirement (ER) during pregnancy and the lactation period for the 19–50 years old women were estimated by following the recommendations of Trumbo et al [48] and presented in Table 1.

Table 1. ER (daily energy requirement) of the pregnant or the lactating women, when calculated as the (ER of the non-pregnant woman) + (additional energy expended during pregnancy) + (energy deposition).

1 st trimester: Adult ER + 0 + 0
2 nd trimester: Adult ER + 160 kcal (8 kcal/week, approximately for 20 weeks) + 180 kcal = 673 kJ (33 kJ/week, approximately for 20 weeks) + 752 kJ
3 rd trimester: Adult ER + 272 kcal (8 kcal/ approximately for 34 weeks) + 180 kcal = 1,137 kJ (33 kJ/week for 34 weeks) + 752 kJ
lactation period: Adult ER of pre-pregnancy + milk energy output
Weight loss calories during the 1 st 6 months after pregnancy: ER + 500 kcal– 170 kcal = ER+2090 kJ – 710 kJ

Table 1 implies that in the second trimesters 160 kcal/day (669 kJ/day) plus 180 kcal/day (752 kJ) of calories and in the third trimester, 272 kcal (1,137 kJ) and 180 kcal/day (752 kJ) of calories should be allocated to the pregnant women. One g of fat corresponds to 9 kcal (38 kJ); therefore, in the formulations 180 corresponds to 20 g of daily fat storage by the pregnant women. The diet therapy used in twin and triplet pregnancies is based on diabetic diet treatment, including three main meals and three snacks per day [48]. During twin breastfeeding, an extra maternal calorie intake of 1,200-1,500 kcal/day (5,016-6,270 kJ/day) is required depending on the production of 1.2-2 L of milk/day. The diet should contain 20% protein, 40% fat and 40% carbohydrate, similar

to the twin pregnancy period [51]. It is also recommended that women with twins consume an additional 50 g/day protein at the beginning of the second trimester [49].

For normal-weight women, the diet list was prepared to comply with the recommendations that the twin-pregnancy weight gain will be between 17-25 kg. This recommended weight gain may be slightly lower for overweight women with 14-23 kg and for obese women with 11-19 kg [52]. The weight gains during pregnancy include the approximate weights of the placenta (1 kg), babies (2.5 kg each), amniotic fluid that surrounds the baby in the womb (1 kg), enlargement of the uterine (1 kg), enlargement of the breast tissue (2 kg), increase in the blood (2 kg), maternal tissue fluids (2 kg) and the rest may be maternal tissue fat stores. Their diet may consist of 20% proteins, 40% carbohydrates, and 40 % fats [48]. The lower carbohydrate percentage provides better glycemic control, and the higher the fat rate provides more calories with less bulk. Low glycemic index carbohydrates in the diet content prevent wide fluctuations in blood glucose concentrations [53]. It was argued that the adequate daily intake of 3,500 kcal (14,630 kJ) composed of 350 g of carbohydrate, 175 g of protein, and 156 g of fat per day for normal-weight women with twins [53].

Low-calorie healthy foods generally cost more than energy dense foods [49,53]; therefore, poor pregnant women are more likely to choose high carbohydrate-containing, energy-dense foods due to their lower price [54]. Low socioeconomic pregnant women's diet may be 300 kcal (1,254 kJ) lower than the healthy pregnant women's diet. The diet of the poor women may consist of 55-60 % carbohydrates, 15-20 % proteins, and 30 % lipids (Rajikan, et al (2017). In poverty, singleton and twin pregnancy diets are 300 kcal (1,254 kJ) less than the diets of a normal healthy pregnant woman. The percentage of macronutrients in the diet; is set to be 55-60% carbohydrate, 15-20% protein, and 30% fat [54]. Nutritional values of the foods used in the menus are taken from USDA Food Composition Data [55].

2.2 Thermodynamic Considerations

Calculations presented in this study consider a 30 years old pregnant woman having her first pregnancy; four different types of diets are designed for each trimester and lactation. A thermodynamic system describing a pregnant or a lactating woman is described in Figure 1.

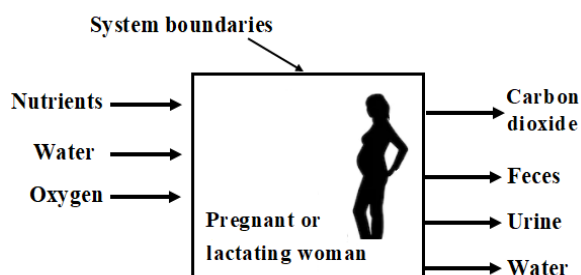
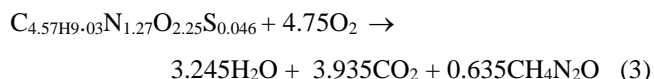
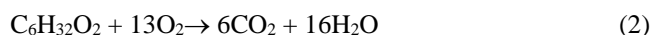


Figure 1. Schematic description of the thermodynamic system boundaries of pregnant woman. Nutrients, water and O_2 are the inputs of the system and products of the metabolism, i.e., water, carbon dioxide and urine and feces are exiting the system.

Equations (1)-(5) are related only with what is happening within the system boundaries, e, g., the woman and the baby. The rest of the universe is outside of the system boundaries and are not the subject of our analyses. For the calculations of total input and output in the body:



Glucose represents carbohydrates, palmitic acid represents lipids, and a mixture of 20 amino acids represents proteins. They are metabolized in the body via O_2 , and they leave as H_2O , CO_2 , and urea (CH_4N_2O). Equations (4) and (5) describe the enthalpy and entropy change of the metabolic reactions and neglect the heat released from the body. Enthalpy change upon the metabolism of glucose, $\Delta h_{metabolism}$, was actually enthalpy change of reaction (1) and calculated as

$$\Delta h_{metabolism} = 6\Delta h_{f,CO_2} + 6\Delta h_{f,H_2O} - \Delta h_{f,C_6H_{12}O_6} - 6\Delta h_{f,O_2} \quad (4)$$

where, $\Delta h_{f,CO_2}$ and $\Delta h_{f,H_2O}$ are the enthalpies of formation of the metabolic products at the body temperature (37 °C), and $\Delta h_{f,C_6H_{12}O_6}$ and $\Delta h_{f,O_2}$ are the enthalpy of formation of the reactants at room temperature (25°C). Thermodynamic data are presented in Table 2.

Specific entropy generation rate from the metabolism of glucose was:

$$\Delta \dot{s}_{rxn} = 6\dot{s}_{CO_2} + 6\dot{s}_{H_2O} - \dot{s}_{C_6H_{12}O_6} - 6\dot{s}_{O_2} \quad (5)$$

where, \dot{s}_{CO_2} and \dot{s}_{H_2O} are the absolute entropy exit rates of the products at body temperature from the metabolism, and $\dot{s}_{C_6H_{12}O_6}$ and \dot{s}_{O_2} are the absolute entropy entrance rates of the reactants at room temperature to metabolism. Equation (5) refers to entropy of the reaction for carbohydrate as described in Eq (1). Similar calculations as those of equations (4) and (5) were also done for the lipid and amino acid utilization in the energy metabolism by replacing the thermodynamic properties of glucose with those of palmitic acid and average amino acid, respectively. We have carried out the calculations for 30 years old healthy and moderately active women. As seen in Table 3, the first, second, third trimester and breastfeeding diet calories employed in this study are 2,000 kcal/day (8,360 kJ/day); 2,350 kcal/day (9,823 kJ/day); 2,450 kcal/day (10,617 kJ/day), and 2,330 kcal/day (9,739 kJ/day), respectively. Diet lists were prepared according to the dietary guidelines presented in the references [48, 49, 51]; then the nutrients provided by these diets are presented in Table 3 to establish the basis for further calculations. In Table 3, if one adds the uptakes and subtracts the amount of products of the metabolism, there would be no mass conservation, since the difference is employed to synthesize the babies and the changes occurring in the body of the mother. The term calculated with equation 5 is actually the rate of entropy change of the chemical reactions representing the human metabolism. Considering the standard definitions of classical thermodynamics, this term would equal the rate of entropy generation only in stationary processes, also neglecting any heat flows. In Table 3, all the women were assumed consuming 2.L of water, every day

and wealthy and the poor women may not be from the same country.

3. Results and Discussion

In the present study, recommendations of the nutritionists are considered while formulating the diets; therefore, all the cases (with the exception of the nutrition of the poor women in case of twin pregnancy) discussed in this study actually lead to optimal entropy generation rates as described in Table 4. Entropy generation reported in this study is actually those of the metabolic reactions. Increase in the weight of the fetus would be the result of larger amounts of nutrients entering in these reactions; therefore, cause an increase in entropy generated by the pregnant women. The fetus gains weight as we go from the first trimester to the second and then to the third trimester Table 4 shows the associated increase in the entropy generation.

Poor women consume more carbohydrate than the recommended level; therefore, their entropy generation rate is not optimal. By following the same procedure as Öngel et al. [29], a telomere length-based energy efficiency factor η is employed while calculating the entropy generation in each stage of the pregnancy and lactation as:

$$\text{Entropy generation rate in each group} = \dot{\Delta}s_{rxn}/\eta \quad (6)$$

and then the total pregnancy and the lactation period entropy generation is calculated as:

total pregnancy and lactation period entropy =

$$\sum(\dot{\Delta}s_{rxn}/\eta)_i(\text{time length of the increment}) \quad (7)$$

where, $\dot{\Delta}s_{rxn}$ is the nutrition-related entropy generation calculated based on equation (5) for carbohydrates or its equivalents for lipids or proteins. Equations (6) and (7), in agreement with the disposable soma theory which states that when the organisms have limited resources the entropy-accumulated, e.g., the damage collected, building blocks, are recycled, by doing so the cells may both get rid of the defective building elements and reuse the energy stored there. According to the Merriam Webster dictionary, “soma” means a part of the body. Although telomere lengths may not have direct correlation with energy efficiency, the shortening of the telomeres goes parallel with the decrease in the energy efficiency.

Telomere length data were adapted from Huang et al [56], as presented in Table 4. The percentage of the entropy generated in the pregnancy and lactation period, when compared to the non-pregnant woman's lifespan entropy is presented in Table 5. In the case of singleton pregnancy, eating less, e.g., in reasonable amounts, leads to smaller amounts of entropy generation; therefore, may be cherished, but in the case of twin pregnancy, eating non-nutritious food in insufficient amounts is something to be avoided. Placenta plays a major role in hormone production during pregnancy [57]. In multiple pregnancies, placental lactogen and progesterone hormone secretion increase more than that of a singleton pregnancy. An increase in these hormones affects glucose metabolism, thus increases the risk of gestational diabetes mellitus and insulin resistance [40].

Multiple pregnancies involve significant maternal physiological changes, including increased plasma volume, increased resistance to carbohydrate metabolism, and increased basal metabolic rate [58]. Only 3% of all births are multiple pregnancies but they account for 20% of low birth-

weight (less than 2,500 g) and 19–24% of very-low-birth-weight (less than 1,500 g) and for 15% of preterm births in the United States [58]. In twin pregnancy, especially in the second half of pregnancy glycogen stores are depleted faster [52].

Maternal resting energy expenditure increases by 10% in twin pregnancies than singleton pregnancies [58]. The diet lists of this study were prepared to address this information. The results of this study should be interpreted with caution, in case of sarcopenia or famine human body may consume its own building blocks in its energy metabolism and such an experience do not extend the lifespan. On the other hand, Ulu et al [59] showed that intermittent caloric restriction via skipping a meal for 30 days in a year without increasing the caloric content of other meals might extend the life span approximately 3%. A high-entropy generation process shortens the expected longevity more than a low-entropy generation process, as evidenced in Table 5. In twin pregnancy, entropy generated in the first trimester is 235 kJ/(kg K) corresponding to 2.1% of the lifespan entropy limit of the non-pregnant woman, whereas entropy generation by non-pregnant women in the same period is 135 kJ/(kg K), corresponding to 1.2% of her lifespan entropy limit. Metabolic entropy generation is not necessarily based on the externally provided nutrients. In case of famine or sarcopenia, human body consumes its own building blocks in its energy metabolism and generate entropy [60]. Such an experience does not contribute to entropy generation only, but also damages the muscles and decreases the muscle work efficiency η_{II} defined in equation 11. Helle and Lummaa [61] after analyzing the data collected in pre-industrial Finland, where conditions were similar to pregnancy and lactation in poverty, reported that the decrease in longevity of the women was related with the number of the pregnancies they had. Since the baby boys had higher body weight at birth than the baby girls, more energy is needed to synthesize them than what is needed for the baby girls; therefore, more entropy is generated in the pregnancies for the baby boys. The decrease in the longevity of the mothers was more striking in the mothers of the baby boys, when compared to those of the baby girls.

The oxidation reaction involves “shuffling” of electrons of the nutrient atoms with those of the oxidizing agent, oxygen, which serve as electron acceptor. Recently the relation between numbers of electron moles transferred to oxygen per mole of fuel is shown to be 4 times of the stoichiometric moles for C-H-O-S fuels [62]. Thus, for carbohydrates, it is 24 electrons/mole; for fat, it is 92 electrons/mole. Each electron mole transfers results in release of 111 kJ/electrons mole [63]. Thus, protein has low metabolic efficiency ($\eta=10\%$) compared to carbohydrates (almost $\eta=40\%$) and fat; therefore, causes higher entropy generation. Protein is used mainly for bodybuilding or replacing cells. Longevity may be assessed according to the Rubner's hypothesis [64] based on the first law limit or according to the Silva's hypothesis, which is based on the second law of thermodynamics. In the present study, the second law analyses are performed. This study was formulated with the same principles as those of Öngel et al [29], Yildiz et al [65,66] and Semerciöz et al [67] and offers thermodynamic assessment to the issue of whether pregnancy affects longevity of the women or not. Todhunter et al [68] achieved documenting the consequences of entropy accumulation in the tissues visually.

Heat released from the body was neglected while establishing equations (4) and (5), based on our discussion of exergy balance in reference [67]. Exergy balance is the of the other way of making second law analysis is as:

$$\sum_{in}[\dot{N} ex]_{in} - \sum_{out}[\dot{N} ex]_{out} - \sum_i[1 - (T_s/T_{b,i})] \dot{Q}_i - \dot{W} - \dot{E}x_{dest} = d[N ex]_{system} / dt \quad (8)$$

when exergy accumulates in the system slowly the right hand side of the equation may be neglected and assumed zero. Traditionally, the “*useful work potential*” of the metabolic heat discarded from the body is assessed in terms of its work potential in a Carnot engine operating between the system and the environment temperatures as “ $\dot{W} = \dot{Q}[1 - (T_r/T_b)]$ ” where, T_b is 310.15 K, i.e., the body temperature on its surface and T_s is the room temperature in the immediate surrounding and taken as the average of the body surface (310.15 K) and the room (298.15 K) temperatures. In the assessments with pregnant mice, the calculated magnitude of \dot{W} was very small; therefore, considered “*not useful for performing work*” [67], implying that neglecting the heat released from the body, do not actually cause a considerable error in the present study. In the present study, entropy generation does not result in increase in the entropy of the body since the body is at steady state. It is like hot water kettle where electric input overcomes heat loss and maintain water at steady temperature. Entropy generated is flushed out. Entropy of water remains constant since water is at steady temperature. However, entropy generated within the body is due to electron transfer and hence the reactive oxidative species damage keeps occurring in proportion to entropy generated [62]. In the present study the telomere shortening was considered within the context of the disposable soma theory and not elaborated further. But, in the literature estrogen levels are reported to be increasing

during the pregnancy [39] and their levels are related with the telomere lengths [69].

4. Conclusion

Our assessment recommends strongly that the women should choose their diets carefully during pregnancy and the lactation stages of their lives to minimize their metabolic entropy generation rates to avoid filling up their lifespan entropy generation limit. Based on the diets designed exclusively for each of them, our assessments showed that a wealthy woman in a singleton pregnancy may generate 1.5% and in the case of twin pregnancy 2.1% of the total lifespan entropy generation by a non-pregnant wealthy woman. A poor woman may generate in the case of the singleton pregnancy 1.8% and in case of the twin pregnancy 2.1% of the total lifespan entropy generated by a wealthy woman. It should be remembered here that; in the multiple pregnancies the babies are usually smaller when compared to those of the singleton pregnancies. If the lifespan of the women should be determined exclusively by the entropic age concept; longevity may exceed 100 years. Under these circumstances the percentages, which are presented here to quantify the effect of the pregnancy and lactation on the lifespan of the women does not appear to be significantly different from each other. Therefore, we may conclude that if the pregnant and the lactating women should have diets designed by knowledgeable nutritionists according to the scientific nutritional recommendations and guidelines. In such a case, the number of the pregnancies they have may not decrease their expected lifespan. In real life, women may not stick to such diet lists; therefore, there may be fluctuations in the observed longevities. The small differences, which are calculated in the present study, may actually explain the reason for conflicting longevity and fertility relations reported in the previous studies.

Table 2. Thermodynamic properties of the nutrients and the products of the metabolism at 1 atm (adapted from Kuddusi, [27]). Where h_i^0 describes the specific enthalpy of formation of the reactants of the metabolism at 273 K, $h_{i,298\text{ K}}$ describes the specific enthalpy of formation of the reactants of the metabolism at body temperature; s_i^0 and $s_{i,310\text{ K}}$ are the absolute entropies of the reactants of the metabolism under the standard conditions and those of the products of the metabolism at the body temperature.

Nutrient	h_i^0 (kJ/kmol) at 273 K	$h_{i,298\text{ K}}$ (kJ/kmol)	$h_{i,310\text{ K}}$ (kJ/kmol)	s_i^0 (kJ/kmol K) at 273 K	$s_{i,310\text{ K}}$ (kJ/kmol K) at 310 K
Glucose (C ₆ H ₁₂ O ₆)	-1260 x 10 ³	-	-	212	
Palmitic acid (C ₁₆ H ₃₂ O ₂)	-835x10 ³	-	-	452.4	
Average amino acid (C _{4.57} H _{9.03} N _{1.27} O _{2.25} S _{0.046})	-385x10 ³	-	-	1.401x119	
O ₂		8,682	-	218.0	
H ₂ O		9,904	-	215.5	219
CO ₂			9,807	240.4	243.6
N ₂			9,014		193.7

Table 3. Calories, the composition of the uptake of the nutrients of and the excreted feces and the urine with each diet in the cases of the pregnancy and lactation of wealthy and poor women for singleton and twin pregnancies.

	1 st trimester diet		2 nd trimester diet		3 rd trimester diet		lactation diet	
	Singleton baby	Twin babies	Singleton baby	Twin babies	Singleton baby	Twin babies	Singleton baby	Twin babies
WEALTHY WOMEN								
Nutrients uptake	2,000 kcal/day (8,360 kJ/day)	2,000 kcal/day (8,360 kJ/day)	2,350 kcal/day (9,838 kJ/day)	3,300 kcal/day (13,794 kJ/day)	2,450 kcal/day (25,090 kJ/day)	3,450 kcal/day (14,421 kJ/day)	2,330 kcal/day (9,838 kJ/day)	3,500 kcal/day (14,630 kJ/day)
Carbohydrate (g/day)	317	200	331	324	329	348	339	362
Fat (g/day)	52	84	75	138	83	154	66	169
Protein (g/day)	73.6	105	96.6	128	100	175	103	149
O ₂ (g/day)	581.5	596	692	904	717.5	1,037	683	1,060
H ₂ O (g/day)	285	270	330	412	340	468	328	480
CO ₂ (g/day)	715	687	832	1,039	857	1,188	828.6	1,210
Feces (g/day)	1,347	840	980	480	921	1,438	877	142
Urine (g/day)	1,201	1,719	1,576	2,086	1,636	2,852	1,681	2,432
POOR WOMEN								
Nutrients uptake	1,700 kcal/day (7,106 kJ/day)	1,700 kcal/day (7,106 kJ/day)	2,050 kcal/day (8,569 kJ/day)	2,800 kcal/day (11,704 kJ/day)	2,150 kcal/day (8,569 kJ/day)	3,000 kcal/day (12,500 kJ/day)	2,050 kcal/day (8,569 kJ/day)	3,200 kcal/day (13,376 kJ/day)
Carbohydrate (g/day)	271	271	260	397	292	398	267	460
Fat (g/day)	47	47	73	85	66	96	75	105
Protein (g/day)	50	50	109	129	83	119	72	98
O ₂ (g/day)	488	488	627	832	607	852	592	917
H ₂ O (g/day)	240	240	292	397	290	405	280	442
CO ₂ (g/day)	599	599	741	1,003	730	1,020	702	1,105
Feces (g/day)	1,787	1,787	774	465	1,200	627	1,377	965
Urine (g/day)	810	810	1,786	2,101	1,350	1,936	1,171	1,591

Table 4. Telomere length (relative units) and entropy generation rate (kJ/K kg) in each trimester and the lactation period.

	1 st trimester	2 nd trimester	3 rd trimester	Lactation period
	Normal pregnancy for a singleton baby			
Telomere length	1.40	1.57	1.57	1.41
Entropy generation rate	2.70x10 ⁻⁶	2.88x10 ⁻⁶	2.98x10 ⁻⁶	3.20x10 ⁻⁶
Entropy generated in pregnancy and lactation	171			

Tubal pregnancy for a singleton baby				
Telomere length	1.54	1.43	1.43	1.47
Entropy generation rate	2.46×10^{-6}	3.16×10^{-6}	3.27×10^{-6}	3.07×10^{-6}
Entropy generated in pregnancy and lactation	171			
Normal pregnancy for twin babies				
Telomere length	1.40	1.57	1.57	1.41
Entropy generation rate	2.83×10^{-6}	3.71×10^{-6}	4.35×10^{-6}	4.84×10^{-6}
Entropy generated in pregnancy and lactation	235			
Tubal pregnancy for twin babies				
Telomere length	1.54	1.43	1.43	1.47
Entropy generation rate	2.57×10^{-6}	4.08×10^{-6}	4.77×10^{-6}	4.64×10^{-6}
Entropy generated in pregnancy and lactation	235			
Normal pregnancy in poverty for a singleton baby				
Telomere length	1.4	1.57	1.57	1.41
Entropy generation rate	2.22×10^{-6}	2.67×10^{-6}	2.52×10^{-6}	2.69×10^{-6}
Entropy generated in pregnancy and lactation	146			
Normal pregnancy in poverty for twin babies				
Telomere length	1.4	1.57	1.57	1.41
Entropy generation rate	2.22×10^{-6}	3.50×10^{-6}	3.53×10^{-6}	4.13×10^{-6}
Entropy generated in pregnancy and lactation	201			
Tubal pregnancy in poverty for a singleton baby				
Telomere length	1.54	1.43	1.43	1.47
Entropy generation rate	2.02×10^{-6}	2.92×10^{-6}	2.76×10^{-6}	2.58×10^{-6}
Entropy generated in pregnancy and lactation	146			
Tubal pregnancy in poverty for twin babies				
Telomere length	1.54	1.43	1.43	1.47
Entropy generation rate	2.02×10^{-6}	3.84×10^{-6}	3.88×10^{-6}	3.97×10^{-6}
Entropy generated in pregnancy and lactation	201			
	A non-pregnant woman, generating entropy in a similar period		A man generating entropy in a similar period	
Telomere length	1.41	1.47	1.42	1.49
Entropy generation rate	2.46×10^{-6}	2.36×10^{-6}	3.52×10^{-6}	3.35×10^{-6}
Entropy generated in pregnancy and lactation	135		1.94	

Table 5. Total and percentage of the entropy generated in the pregnancy and lactation period when compared to the non-pregnant woman's lifespan entropy. We performed the calculations according to the dietary guidelines [48], which do not require a specific weight; the results are applicable to 60 kg, 170 cm tall women.

	Total entropy generation during pregnancy and lactation period [kJ/(K kg woman)]	Percentage of the non-pregnant woman's lifespan entropy (%)	Total entropy generation during pregnancy and lactation period [kJ/(K kg woman, kg)]	Percentage of the non-pregnant woman's lifespan entropy (%)
	NP		TP	
Singleton pregnancy	171	1.5	171	1.5
Twin pregnancy	235	2.1	235	2.1
Singleton pregnancy in poverty	146	1.3	146	1.3
Twin pregnancy in poverty	201	1.8	201	1.8
Non-pregnant women	135	1.2		
Men	194	1.7		

Nomenclature

h_i^0 specific enthalpy of formation at 273 K, (kJ/kmol)

h_i $_{,298\text{ K}}$ specific enthalpy of formation at body temperature (kJ/kmol)

s_i^0 absolute entropy the standard conditions (kJ/kmol K)

s_i $_{,310\text{ K}}$ absolute entropy at the body temperature (kJ/kmol K)

References

- [1] O. Toussaint, C. Michels, M. Raes and J. Meracle. "Cellular aging and the importance of energetic factors". *Exp. Gerontol.* 30(1), 1-22, 1995; doi:10.1016/0531-5565(94)00038-5.
- [2] T. Nyström., "A bacterial kind of aging". *PLoS Genet.* 3(12), 2355-2357, 2007; doi:10.1371/journal.pgen.0030224.
- [3] J.A. Joseph, N. Denisova, D. Fisher, B. Shukitt-Hale, B. Bickford, R. Prior, and G. Cao. "Age-related neurodegeneration and oxidative stress: putative nutritional intervention." *Neurol Clin* 16(3):747-755, 1998; doi:10.1016/S0733-8619(05)70092-X.
- [4] H. Giese, W.K. Snyder, C. van Oostrom, H. van Steeg, M.E.T. Dolle and J. Vijg. "Age related mutation accumulation at lacZ reporter locus in normal and tumor tissues of Trp53-deficient mice". *Mutat. Res.* 514, (1-2), 153-163, 2002; doi:10.1016/S1383-5718(01)00329-1.
- [5] M.G. Kosmadaki and B.A. Gilhrest. "The role of telomeres in skin aging/photoaging". *Micron*, 35(3), 155-159, 2004; doi:10.1016/j.micron.2003.11.002.
- [6] S. Sandal, B. Yilmaz, and D.O. Carpenter. "Genotoxic effects of PCB 52 and PCB 77 on cultured human peripheral lymphocytes". *Mutat. Res.*, 654, 88-92, 2008; doi:10.1016/j.mrgentox.2008.05.005.
- [7] A. Salminen, and K. Kaarniranta, K. "Genetics vs. entropy: longevity factors suppress the NF- κ B-driven entropic aging process". *Ageing Res. Rev.* 9(3),298-314,2010; doi:10.1016/j.arr.2009.11.001.
- [8] F. Mete, E. Kilic, A. Somay, A. and Yilmaz, B. (2012). "Effects of heat stress on endocrine functions and behaviour in the pre-pubertal rats". *Indian J. Med. Res.*, Feb., 135, 233-239.
- [9] P.C.W. Davies, E. Rieper and J.A. Tuszynski, J.A. "Self-organization and entropy reduction in a living cell". *BioSystems*, 111(1), 1-10, 2013; doi:10.1016/j.biosystems.2012.10.005.
- [10] P. Lenart and J. Bienertova-Vasku (2016). Double strand breaks may be a missing link between entropy and aging. *Mech. Ageing Dev.* 157, 1-6, 2016; doi:10.1016/j.mad.2016.06.002.
- [11] A.J. Hulbert, R. Pamplona, R. Buffenstein, et al. "Life and death: Metabolic rate, membrane composition, and life span of animals." *Physiol Rev*, 87(4):1175-1213, 2007; doi:org/10.1152/physrev.00047.2006.
- [12] T. Farooqui and AA. Farooqui AA. "Aging: an important factor for the pathogenesis of neurodegenerative diseases." *Mech Ageing Dev*, 130(4):203-215, 2009; doi:org/10.1016/j.mad.2008.11.006.
- [13] C. Yildiz V.A. Bilgin, B. Yilmaz and Özilgen M. "Organisms live at far-from-equilibrium with their surroundings while maintaining homeostasis, importing exergy and exporting entropy." *Int J Exergy*, 31(3): 287-300, 2020; doi:10.1504/IJEX.2020.106457.
- [14] L. Hayflick. "Aging: The reality: "Anti-aging" is an oxymoron." *J. Gerontol. A Biol. Sci. Med. Sci.* 59(6): B573-B578, 2004; doi:org/10.1093/gerona/59.6.B573.
- [15] L. Hayflick. "Biological aging is no longer an unsolved problem." *Ann. NY Acad. Sci.* 1100 (1): 1-13,2007; doi:10.1196/annals.1395.001.
- [16] L. Hayflick. "Entropy explains aging, genetic determinism explains longevity, and undefined terminology explains misunderstanding both." *PLoS Genet.* 3(2): 2351-2354, 2007; doi:10.1371/journal.pgen.0030220.
- [17] C.A. Silva and K. Annamalai. "Entropy generation and human aging: Lifespan entropy and effect of physical activity level." *Entropy*, 10: 100-123, 2008; doi:org/10.3390/entropy-e10020100.
- [18] C.A. Silva and K. Annamalai. "Entropy generation and human aging: lifespan entropy and effect of diet composition and caloric restriction diets," *J. Thermodyn.* 2009(186723), 1-10, 2009; doi:10.1155/2009/186723.
- [19] K. Annamalai and C.A. Silva. "Entropy stress and scaling of vital organs over life span based on allometric laws." *Entropy* 14(12): 2550e77, 2012; https://doi.org/10.3390/e14122550.
- [20] E. Schrödinger. "What is life? The physical aspects of a living cell". Cambridge University Press, Cambridge, 1944.
- [21] I. Prigogine, J. Wiame. "Biologie et thermodynamique des phénomènes irréversibles." *Experientia*, 2(11): 451-453, 1946; doi:10.1007/BF02153597.
- [22] B.H. Yaçınkaya, S. Genc, J. Çatak, M. Özilgen and B. Yilmaz. "Mitochondrial Energy Conversion" in "Comprehensive Energy Systems" I. Dincer, (Editor), Elsevier, February 21, 2018.
- [23] R. Jumpertz, R.L. Hanson, M.L. Sievers, P.H. Bennet, R.G. Nelson and J. Krakoff." Higher energy expenditure in humans predicts natural mortality." *J. Clin. Endocrinol. Metab.*, 96(6): E972-976, 2011; doi:10.1210/jc.2010-2944.
- [24] C.K. Martin, L.K. Heilbronn, L. de Jonge, J.P. DeLany, J. Volaufova, S.D. Anton, L.M. Redman, S.R. Smith and E. Ravussin. "Effect of calorie restriction on resting metabolic rate and spontaneous physical activity." *Obesity (Silver Spring)*; 15(12):2964-2973, 2007; doi: 10.1038/oby.2007.354.
- [25] S.B. Roberts, P. Fuss, W.J. Evans, M.B. Heyman and V.R. Young. "Energy expenditure, aging and body composition." *J. Nutr.*123(2 suppl):474-480, 1993; doi:10.1093/jn/123.suppl_2.474.
- [26] L. Fontana. "The scientific basis of caloric restriction leading to longer life." *Curr. Opin. Gastroenterol.*, 25:144-150, 2009; doi:10.1097/MOG.0b013e32831ef1ba.

- [27] L. Kuddusi. "Thermodynamics and life span estimation." *Energy*; 80:227-238, 2015; doi:org/10.1016/j.energy.2014.11.065.
- [28] A.K. Patel and S.P.S. Rajput. "Thermodynamic life cycle assessment of humans with considering food habits and energy intake." *Saudi J. Biol. Sci.* 28:531-540, 2021; doi:org/10.1016/j.sjbs.2020.10.038.
- [29] M.E. Öngel, C. Yildiz, C. Akpınaroğlu, B. Yilmaz, M. Özilgen. "Why women may live longer than men do? A telomere-length regulated and diet-based entropic assessment." *Clin. Nutr.* 40(3): 1186-1191, 2020; doi:10.1016/j.clnu.2020.07.030.
- [30] R.J. Hodes. "Telomere length, aging and somatic cell turnover." *J. Exp. Med.*, 190(2): 153–156, 1999; doi:10.1084/jem.190.2.153.
- [31] A. Muezzinler, A.K. Zaineddin and H.A. Brenner "Systematic review of leukocyte telomere length and age in adults." *Ageing. Res. Rev.*, 12(2): 509-519, 2013; doi:10.1016/j.arr.2013.01.003.
- [32] C. Massafra, D. Gioia, C. De Felice, E. Picciolini, V. De Leo, M. Bonifazi and A. Bernabei. "Effects of estrogens and androgens on erythrocyte antioxidant superoxide dismutase, catalase and glutathione peroxidase activities during the menstrual cycle." *J. Endocrinol.*, 167, 447–452, 2000; doi:10.1677/joe.0.1670447.
- [33] T.L.B. Kirkwood. "Evolution of ageing, *Mechanisms of ageing and development.*" 123 (7): 737-745, 2002; doi:org/10.1016/S0047-6374(01)00419-5.
- [34] S. Casagrande and M. Hau. "Telomere attrition: Metabolic regulation and signalling function?" *Biol. Lett.*, 15(3): 20180885, 2019; doi:10.1098/rsbl.2018.0885.
- [35] D.T.A. Eisenberg. "An evolutionary review of human telomere biology: The thrifty telomere hypothesis and notes on potential adaptive paternal effects." *Am. J. Hum. Biol.*, 23(2): 149–167, 2011; doi:org/10.1002/ajhb.21127.
- [36] S.B. Roberts and W.A. Coward. "Lactation increases the efficiency of energy utilization in rats." *J. Nutr.*, 114(12):2193-200, 1984; doi:10.1093/jn/114.12.2193.
- [37] S.B. Roberts, T.J. Cole and W.A. Coward. "Lactational performance in relation to energy intake in baboon." *Am. J. Clin. Nutr.*, 41(6):1270-1276, 1985; doi:10.1093/ajcn/41.6.1270.
- [38] Knopp HR. Hormone-mediated changes in nutrient metabolism in pregnancy: A physiological basis for normal fetal development, *Ann NY Acad Sci*, 1997;817, 251-271; doi:10.1111/j.1749-6632.1997.tb48212.x.
- [39] L. Bernstein, L. Lipworth, R.K. Ross and D. Trichopoulos. "Correlation of estrogen levels between successive pregnancies." *Am. J. Epidemiol.*, 142(6), 625-628, 1995; doi:10.1093/oxfordjournals.aje.a117685.
- [40] M.E. Rosello-Soberon, L. Fuentes-Chaparro and E. Casanueva. "Twin pregnancies: Eating for three? Maternal nutrition update." *Nutr. Rev.* 63(9), 295–302, 2005; doi:10.1111/j.1753-4887.2005.tb00144.x.
- [41] F.J. Darne, H.H. McGarrigle and G.C. Lachelin. "Diurnal variation of plasma and saliva oestrogen, progesterone, cortisol and plasma dehydroepiandrosterone sulphate in late pregnancy." *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 32(2): 57-66, 1989; doi:10.1016/0028-2243(89)90184-6.
- [42] M.A. Kominiarek and P. Rajan. "Nutrition recommendations in pregnancy and lactation." *Med. Clin. North Am.*, 100 (6): 1199–1215, 2016; doi:10.1016/j.mcna.2016.06.004.
- [43] R.G.J. Westendorp and T.B.L. Kirkwood "Human longevity at the cost of reproductive success." *Nature*, 396, 743-746, 1998; doi:10.1038/25519.
- [44] K.R. Smith, G.P. Mineau and L.L. Bean "Fertility and post-reproductive longevity." *Soc. Biol.* 49(3-4):185–205, 2010; doi:10.1080/19485565.2002.9989058
- [45] J.E. Lycett, R.I.M. Dunbar and E. Voland. "Longevity and the costs of reproduction in a historical human population." *Proc. R. Soc. Lond. B Biol Sci*, 267(1438):31-35, 2000; doi:10.1098/rspb.2000.0962.
- [46] C-H. Hsu, O. Posegga, K. Fischbach and H. Engelhardt. "Examining the trade-offs between human fertility and longevity over three centuries using crowdsourced genealogy data." *PLoS One*, 16(8): e0255528, 2021; doi:10.1371/journal.pone.0255528
- [47] DGA. "2020-2025 dietary guidelines for Americans," US Department of Health and Human Services and US Department of Agriculture, December 2020.
- [48] P. Trumbo, S. Schlicker and Yates AA, et al. "Food and Nutrition Board, Institute of Medicine: Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids." National Academies Press Washington, DC, 2002.
- [49] P. Monsivais and A. Drewnowski. "The rising cost of low-energy-density foods." *J. Am. Diet. Assoc.* 107(12), 2071-2076, 2007; doi:10.1016/j.jada.2007.09.009.
- [50] R. Elango and R.O Ball. "Protein and amino acid requirements during pregnancy." *Adv. Nutr.* 7(4), 839S-844S, 2016; doi:org/10.3945/an.115.011817).
- [51] IOM and NRC. Institute of Medicine (US) and National Research Council (US) Committee to reexamine IOM pregnancy weight guidelines. "Weight gain during pregnancy: Reexamining the guidelines." K.M. Rasmussen and A.L. Yaktine. (editors). National Academies Press, Washington DC, 2009.
- [52] B. Luke. "Nutrition and multiple gestation." *Semin. Perinatol*, 29, 349-354; 2005; doi:10.1053/j.semperi.2005.08.004.
- [53] S. Kish. "Healthy, low calorie foods cost more on average," available at <https://naldc.nal.usda.gov/download/15381/PDF>; accessed February 6, 2021.
- [54] R. Rajikan, N.S.A. Zaidi, S.M. Elias. "Construction of healthy and palatable diet for low socioeconomic female adults using linear programming." *Int J Adv Sci. Eng. Inf. Techno.* 7(1), 125-131, 2017; doi:10.18517/ijaseit.7.1.1191.

- [55] USDA (2021). "Food composition database." Available at <https://fdc.nal.usda.gov>; accessed: 03.02.2021.
- [56] Z. Huang, X. Zhao, H. Zhang, G. Liang, H. Qi, X. He C, Zhu, S. Ge and J. Zhang. "The association between mitochondrial DNA copy number, telomere length, and tubal pregnancy." *Placenta*, 97: 108–114, 2020; doi:10.1016/j.placenta.2020.06.017.
- [57] T. Napso, H.E.J. Yong, J. Lopez-Tello, and A.N. Sfruzzi-Perri AN. "The role of placental hormones in mediating maternal adaptations to support pregnancy and lactation." *Front. Physiol.* 9(1091), 1-39, 2018; doi:10.3389/fphys.2018.01091.
- [58] W. Goodnight and R. Newman. "Optimal nutrition for improved twin pregnancy outcome." *Obstet Gynecol*, 114 (5), 1121-1134, 2009; doi:10.1097/AOG.0b013e3181bb14c8.
- [59] G. Ulu, A.S. Semerciöz, and M. Özilgen. "Energy storage and reuse in biological systems: Case studies." *Energy Storage*, e253, 2021; doi:org/10.1002/est2.253.
- [60] A.J. Cruz-Jentoft, G. Bahat, J. Bauer J. et al. "Sarcopenia: Revised European consensus on definition and diagnosis." *Age Ageing*, 48(1), 16–312, 2019; doi:10.1093/ageing/afy169.
- [61] S. Helle and V. Lummaa. "A trade-off between having many sons and shorter maternal post-reproductive survival in pre-industrial Finland." *Biol. Lett.*, 9, 20130034, 2013; <http://dx.doi.org/10.1098/rsbl.2013.0034>.
- [62] K. Annamalai. "Oxygen deficient (OD) combustion and metabolism: Allometric laws of organs and Kleiber's law from OD metabolism?" *Systems* 9, 54, 2021; doi:org/10.3390/systems 9030054.
- [63] M. Popovic. "Thermodynamic properties of microorganisms: Determination and analysis of enthalpy, entropy, and Gibbs free energy of biomass, cells and colonies of 32 microorganism species." *Heliyon* 5, e0195, 2019; doi:10.1016/j.heliyon.2019.e01950
- [64] M. Rubner. Machinery of metabolism, *J. Am. Med. Assoc.* 66(24):1879, 1916.
- [65] C. Yildiz C, M.E. Öngel, B. Yilmaz, and M. Özilgen. "Diet-dependent entropic assessment of athletes' lifespan." *J. Nutr. Sci.* 10, E-83, 2021; doi:10.1017/jns.2021.78.
- [66] C. Yildiz, S.A. Semerciöz, B.H. Yalçinkaya, T.D. Ipek TD, E. Ozturk- Isik, and M. Özilgen. "Entropy generation and accumulation in biological systems." *Int J Exergy* 33(4), 444-468, 2020; doi:10.1504/IJEX.2020.111691.
- [67] A.S. Semerciöz, B. Yilmaz and M. Özilgen. "Thermodynamic assessment of the allocation of the energy and exergy of the nutrients for the life processes during pregnancy." *Br J Nutr* 2020;124(7), 742-753; doi:org/10.1017/S0007114520001646.
- [68] M.E. Todhunter R.W. Sayaman, M. Miyano and M.A. LaBarge. "Tissue aging: The integration of collective and variant responses of cells to entropic forces over time." *Curr Opin Cell Biol*; 54, 121–129, 2018; doi:org/10.1016/j.ceb.2018.05.016.
- [69] Y-A. Shin and K-Y Lee. "Low estrogen levels and obesity are associated with shorter telomere lengths in pre-and postmenopausal women" *J Exerc. Rehabil.*, 12(3): 238 – 246, 2016; doi:org/10.12965/jer.1632584.292.