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Second law efficiency for living cells

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1. ABSTRACT

The exergetic analysis of the biosystems is developed. It takes into account that cells are able to convert only part of the energy absorbed. The result is to highlight the fundamental role of the exergy as a quantity useful to develop considerations on the cells behavior in relation to normal or disease states.

2. INTRODUCTION

The biophysical and biochemical analysis of proteins and DNA allow us to describe the structural properties in relation to intermolecular forces, highlighting that “as the systems become more complex, it is progressively harder to unravel the physical principles behind their functioning” (1), with the consequence that it is too complex for present computer simulations.

Moreover, electrostatic interactions on the nanoscale are often the dominant forces acting between many constituent of living systems in the 1–3 nm prior to surface–surface contact, governing their spontaneous assembly and long range spatial ordering (1).

The bioenergetic studies highlight that biological systems convert energy in the most efficient way for transport of substances across cell membrane (2). From a thermodynamic point of view it means that the biological systems are open systems operating with optimized cycles; so, we can state that these systems convert the maximum energy from one to another form in the least time. From a biological point of view it means that the biological systems behaves in two different way (2,3): 1) the evolution towards maximum disorder; 2) the spontaneous maintenance of a high degree of organization in space and time.

To do so, living systems need to couple metabolic and chemical reactions with transport processes (2-12). Consequently, biological systems are no more than non-equilibrium open systems with irreversible physical and bio-chemical processes (transport of matter, energy and electricity) (2,13-16).

When different phenomena occur simultaneously they may couple generating new effects, as, for example, the transport of a substrate against the direction imposed by the electrochemical potential gradient, known as active transport.

In this paper we review and summarize the exergetic analysis of a biosystem, with particular interest to cell.

3. THE BIOPHYSICAL AND BIOCHEMICAL APPROACH: THERMODYNAMIC CONSIDERATIONS

Dissipation has always been analyzed using the second law of thermodynamics (17-21), based on the study of irreversibility by entropy generation and the availability (often named exergy, which is the energy really used by the system during a process) (16-29).

So, a system, capable of assuming many conformations, will tend to assume the one, or frequently returns to the one, that maximizes the dissipation (2,8-12). Consequently, the exergy gradients can be considered the motive forces of the physical chemical processes (16,30-32), and the entropy generation results the quantity useful to evaluate the irreversibility occurred in the process followed (16,28,29,33).

So, entropy is a fundamental concept to understand thermodynamic aspects of self-organization, evolution of order and life as we observe it in Nature (34).

Entropy is no more than a parameter characterizing the thermodynamic state and the term due to internal irreversibility, S_g, measures how far the system is from the state that will be attained in a reversible way (16): nothing is really *produced* or *generated* (29,35).

The analyses of the living systems have pointed out that the condition of their existence as follows (2,4,5,8-10):

1. there are the possibility to convert an exergy source to entropy;
2. they are in a state far-from-thermodynamic equilibrium;
3. they are composed of subsystems.

Consequently, life is an organizational process, result of system cooperation between components, with an interconnection between sub-systems and super-systems, such that for survival the super-system must export equal or more entropy products than its sub-systems produces, towards maximum conversion of available exergy sources to entropy products (2,4,5,8-10). The biochemical reactions produce or consume external metabolites, accumulated inside the system, and they connect internal metabolites, in constant concentrations in the cells at their steady states (2,4,5,8-10). So, living systems must exchange exergy (available and useful energy) and matter through its boundary, resulting a far-from-equilibrium dissipative thermodynamics systems. The cells reach their optimality by means of a redistribution of the flow pattern through the metabolic network using the pattern of catalytic and regulatory proteins; indeed, mutations and genetic rearrangements are fundamental for an organism to adapt to environmental conditions (2,4,5,8-10). Consequently, from a thermodynamic point of view, a living system (2,4,5,8-10):

1. is open, because it exchanges energy and mass flows through its boundaries;
2. is far-from-equilibrium, because it is a source of high exergy values and basic materials;
3. is on autopoietic pathways, because there exists continuous cycles for generation and autocatalytic feedbacks;
4. has exergy enhancement or maintenance, because it exports entropy products which exceeds or equals the entropy production of the ingested free energy source and it decreases its internal entropy;
5. presents material conservation and maintains its physical components, because it maintains its structural basis for storing the acquired organizational exergy.

The exergy gradients are the sources of physical processes. Entropy quantifies the system's evolution toward increasingly more probable states, while entropy generation describes its irreversibility (2,4,5,8-10), in relation to its causes, which can be summarized as (4,5,8-10):

1. the thermal flux driven by temperature difference, which holds the entropy component $S_{g,tf}$
2. the diffusion current driven by chemical potential gradients, which holds the entropy component $S_{g,dc}$
3. the velocity gradient coupled with viscous stress, which holds the entropy component $S_{g,vg}$
4. the chemical reaction rate driven by affinity, which holds the entropy component $S_{g,cr}$
5. the dissipation due to work by interaction with the environment, which holds the entropy component $S_{g,de}$

Any process occurs in a particular time, its lifetime τ_i (35). The total entropy generation results. $S_g = S_{g,tf} + S_{g,dc} + S_{g,vg} + S_{g,cr} + S_{g,de}$.

Cells are chemical engine in which specific ordered chemical reactions occur. Using the results previously summarized and considering that human organs are at rest and non considering external fields in interaction with them, the entropy generation has been evaluated (4,5,8-10): in relation to the ability of the cell to store energy (entropy generation related to viscous stress can be neglected) and without any external field, the entropy generation results (4,5,9) $S_g = S_{g,dc} + S_{g,cr}$:

$$S_g \approx \frac{\dot{x}_{th} V}{T} \frac{\sum_i \rho_i \left(\mu_{i,os} - \mu_{i,is}\right)}{d_m} \tau_{dc} + V \tau_{cr} \sum_i N_i \frac{\mathcal{A}_i}{T} \quad (1)$$

where:

1. τ_{dc} is the lifetime of this process, V and d_m are the volume and depth of the membrane, where the chemical potential gradient, $\Sigma_i \rho_i(\mu i, os-\mu_{i,is})/d_m$, especially occurs in cytoplasm, $\dot{X}_{th}$ is the thermal velocity, ρ_i is the concentration of the *i*-th species and *os* and *is* means respectively *outside* and *inside* the cell, while T is the mean temperature of the membrane;

2. τ_{cr} is the lifetime of this process, N is the number per unit time and volume of the *i*-th chemical reaction and A is the affinity, evaluated as the variation of the standard Gibbs' free energy.

Now, considering that the entropy generation is always positive and that any process occurs in the least time (maximum entropy generation rate), it follows (9) that:

$$\begin{aligned} & S_g > 0 \Rightarrow \sum_i N_i \mathcal{A}_i > -\dot{x}_{th} \frac{\sum_i \rho_i \left(\mu_{i,os} - \mu_{i,is}\right)}{d_m} \frac{\tau_{dc}}{\tau_{cr}} \\ & \frac{\partial S_g}{\partial t} \geq 0 \Rightarrow \sum_i N_i \mathcal{A}_i \geq -\dot{x}_{th} \frac{\sum_i \rho_i \left(\mu_{i,os} - \mu_{i,is}\right)}{d_m} \\ & \sum_i N_i \mathcal{A}_i \geq 0 \end{aligned} \qquad (2)$$

that at the stationary state holds (9):

$$\tau_{dc} = \tau_{cr} \qquad (3)$$

which means that the time of chemical reaction is equal to the time of chemical diffusion. Moreover, by evaluating the maximum entropy generation rate it follows:

$$\frac{d\Delta T}{dL} + \frac{2}{L}\Delta T = \frac{\xi}{\alpha}\frac{1}{L^2} - 3\frac{\beta}{\alpha} \qquad (4)$$

where:

1. $\alpha = \dfrac{u\dot{x}_{th}}{6T^2}\tau_{tf}$
2. $\beta = \dfrac{\dot{x}_{th}}{T}\dfrac{\sum_i \rho_i \left(\mu_{i,os} - \mu_{i,is}\right)}{d_m}\tau_{dc}$
3. $\xi = \tau_{cr}\sum_i N_i \dfrac{\mathcal{A}_i}{T}$

The solution of the equation (4) results:

$$\Delta T - \frac{L_0^2}{L^2}\Delta T_0 = -\frac{\xi}{\alpha}\left(\frac{1}{L} - \frac{1}{L_0}\right) - \frac{\beta}{\alpha}\left(L - L_0\right) \qquad (5)$$

with L_0 the initial diameter of the daughter cell and ΔT_0 the temperature difference between the cell and environment at the beginning of the any cycle ($L = L_0$). It is possible to highlight that the relation (5) can express also the growth as a function of $\Delta T - \Delta T_0$. This means that this quantity can perform an important role in the diseases related to the cell growing. Cells must maintain their temperature by using some internal metabolic processes against the dissipation with the environment. The first theoretical model of heat transfer in biological tissues was introduced by Penns in 1948 and it is named the bio-heat transfer equation, which can be written as follows (37):

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot \left(\boldsymbol{\lambda} \cdot \nabla T\right) + \omega \rho_b c_b \left(T_b - T\right) + q_m \qquad (6)$$

where ρ is the mass density, *c* is the specific heat, *T* is the temperature, λ is the heat conductivity tensor, ï is the perfusion component, *b* means blood and q_m is the metabolic heat generated by the tissue.

In 1980, Chen and Holmes improved this approach obtaining a more complex model, which requires a great number of numerical values for the bio-physical quantities used. But, it is often difficult to collect and obtain these values. Here, we want to highlight the need to develop a bio-metrology. Their equation can be written as (38):

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot \left(\boldsymbol{\lambda} \cdot \nabla T\right) + \nabla \cdot \left(\boldsymbol{\lambda}_p \cdot \nabla T\right) + \omega \rho_b c_b \left(T_b - T\right) + \rho_b c_b \overline{\mathbf{u}} \cdot \nabla T + q_m \qquad (7)$$

where ū is the diffusion velocity of the blood into the tissues and λ_p is the perfusion conductivity tensor, defined as (38):

$$\boldsymbol{\lambda}_p = n \rho_b c_b \pi r_b^2 \overline{\mathbf{v}} \cos^2 \gamma \sum_{i=1}^{\infty} \frac{L_e}{L_e^2 \beta_i^2 + 1} \qquad (8)$$

where v̄ is the local mean velocity of blood, g is the angle between the blood movement direction and the temperature gradient, *n* is the number of vessels, r_b is the mean radius of the vessel under consideration, L_e is the relative distance between two vessels, β is the Fourier spectral wave number, about the inverse of the vessel length. In this model the more difficult term to be studied is the perfusion conductivity. This makes difficult the use of this mathematical model.

Consequently, it is useful to use other advanced, but less complex, model, as the Weinbaum-Jiji-Lemons one. Its bases are the following two considerations:

1. the tissue temperature can be obtained by taking into account the mean value of the difference of temperature of the arterial and venous vessels in the tissue considered;
2. the heat transfer is mainly conductive.

The equation obtained by Weinbaum, Jiji and Lemons is (39):

$$\rho c \frac{\partial T}{\partial t} = \nabla \cdot \left(\boldsymbol{\lambda}_{eff} \cdot \nabla T\right) + q_m \qquad (9)$$

which represents no more than a Fourier equation with internal heat generation with effective conduction coefficient λ_{eff} defined as (39):

$$\boldsymbol{\lambda}_{eff} = \left[1 + \frac{n\left(\pi\, r_a^2 \rho_b c_b\, \bar{\mathbf{v}} \cos\gamma\right)^2}{\sigma\,\lambda^2}\right]\boldsymbol{\lambda} \qquad (10)$$

where σ is a term which allows us to take into account of the geometry of the system. This model can be used under the limit $L_e/r_a << 1$. This model can be used only for local applications, but it is just what the analysis of cryosurgery requires.

The system must convert exergy in order to supply the energy lost by heat exchange. The exergy of a system is defined as the maximum shaft work that could be done by the composite of the system and a specified reference environment that is assumed to be infinite, in equilibrium, and ultimately to enclose all other systems: the environment is specified by stating its temperature, pressure and chemical composition (36). Exergy is not simply a thermodynamic property, but rather it is related to the reference environment (19). Exergy allows us to evaluate the maximum amount of work which can be produced by a system or a flow of matter or energy as it comes to equilibrium with a reference environment. Exergy is a measure of the potential of the system or flow to cause changes, as a consequence of not being completely in a stable equilibrium relative to the reference environment. Maximal possible conversion of heat Q to work W, known as exergy content of heat, depends on the temperature T at which heat is available and the temperature level T_0 at which the reject heat can be disposed, that is the temperature of the surrounding. The upper limit for conversion is the Carnot efficiency $1 - T_2/T_1$, where T_1 and T_2 are, respectively, the higher and lower temperature of the transformation considered (19). Now, considering the exergy rate $\dot{B}_w$ for an open irreversible system (19):

$$\dot{B}_W = -\frac{d}{dt}\left(E + p_0 V - T_0 S\right) + \sum_{i=1}^{n}\left(1 - \frac{T_0}{T_i}\right)\Phi + \sum_{in} G_{in}\left(h - T_0 s\right)_{in} - \sum_{out} G_{out}\left(h - T_0 s\right)_{out} - T_0 \dot{S}_g \qquad (11)$$

where E is the energy, p is the pressure, T is the temperature, S is the entropy, Φ is the heat power, G is the mass flow, h is the specific enthalpy, s is the specific entropy, 0 means ambient, $i \in (1,n)$ the i-th thermal source, *in* inflow, *out* outflow and S_g is the entropy generation.

Considering that the system tries to supplies in the shorter time the exergy lost, it has been proven that (40):

$$\frac{dB}{dT} = -\frac{\dfrac{T_0}{T^2}}{1 - \dfrac{T_0}{T}} B \qquad (12)$$

so:

1. if $T > T_0$ then $dB/dT < 0$ and $dB/d\tau$ represents the maximum power generated during the process;
2. if $T < T_0$ then $dB/dT > 0$ and $dB/d\tau$ represents the minimum power required during the process.

Now, integrating the equation (12), it follows:

$$B_2 = \frac{1 - \dfrac{T_0}{T_2}}{1 - \dfrac{T_0}{T_1}} B_1 \qquad (13)$$

where 1 means before the metabolic synthesis and 2 after the metabolic synthesis. The results have been experimentally proven (41).

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