Formalization of common power and efficiency definitions for energy-converting intracellular biochemical processes

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The definitions of power and efficiency for energy-converting intracellular biochemical processes, introduced by Caplan and Essig are studied. These definitions are recovered in the present work with the formalism of De Groot and Mazur for First-Order Irreversible Thermodynamics, rather than the formalism of Prigogine, as done by Caplan and Essig. The approach here employed permits to keep track of all the assumptions in a more clear manner, and to get rid of a very strong restriction in the approach of Caplan and Essig which assumes that the chemical potentials are homogeneous inside the cell.

Keywords: Biophysics; irreversible thermodynamics; bioenergetics

Se estudian las definiciones de potencia y eficiencia para procesos bioquímicos intracelulares convertidores de energía, introducidas por Caplan y Essig. En el presente trabajo, dichas definiciones se recuperan usando el formalismo de De Groot y Mazur para la termodinámica irreversible de primer orden, en vez del formalismo de Prigogine, empleado por Caplan y Essig. El punto de vista empleado en el presente manuscrito permite seguir las suposiciones hechas de una manera más clara, además de que hace innecesaria una suposición bastante fuerte usada por Caplan y Essig, la cual da por hecho que los potenciales químicos son homogéneos en el interior de la célula.

Descriptores: Biofísica; termodinámica irreversible; bioenergética

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1. Introduction

According to Luria [1], the main theoretical foundations of Biology are the theory of evolution, the cell theory, and the biochemical unity. Cell theory states that all living beings are made up of cells or, at least, they need of cells for survival and/or reproduction. Even viruses confirm this theory since, although they are not made up of cells, they need of cells for reproduction. The existence of cells satisfies the necessity of keeping concentration of essential materials high enough, so that biochemical reactions can take place at near optimum rates, even when the external concentrations are too low or too high. For this, cells have membranes, which by means of selective pumps and channels retain and even concentrate chemical compounds. For such a reason is that it is convenient to take the cell interior as an open system (one that can exchange mass and energy with the environment) to study it from a thermodynamic point of view.

The concepts of power and efficiency are essential in the study of the energetics of any kind of energy-converting process. Caplan and Essig [2] introduced definitions of power and efficiency for energy-converting intracellular biochemical processes. Although not clearly stated, the definitions of Caplan and Essig rely upon the assumptions that the temperature, the pressure and the chemical potential of all the chemical species, remain constant in time and homogeneous inside the cell.

The local equilibrium hypothesis states that for mesoscopic systems (those for which the thermodynamic variables can be defined locally) the local variables are related in the same manner as the equilibrium ones. This assumption permits to define the entropy as a function of these local variables trough the Gibbs relation. The feasibility of employing the local equilibrium hypothesis, and all its consequences, in the study of biological processes has been widely discussed [2–5]. For the purpose of the present work, we will assume that such hypothesis holds true. Under that assumption, the constancy in time of all the thermodynamic quantities is in agreement with the commonly accepted homeostatic intracellular conditions [6]. The homogeneity of the pressure and the temperature inside the cell are also commonly accepted facts, given that the always present flows of matter and heat are most of the time small enough so they do not alter the intracellular hydrostatic condition. Nevertheless, the chemical potentials can hardly be considered to be homogeneous. This last statement is a weaknesses of the definitions of Caplan and Essig.

In the present work, definitions of power and efficiency for energy-converting intracellular biochemical processes are obtained with the formalism of De Groot and Mazur for First-Order Irreversible Thermodynamics (FOIT), rather than the formalism of Prigogine [3], as done by Caplan and Essig. As far as we are concerned, the approach of the present work has

the advantages of making clear all the assumptions it relies upon, and of making unnecessary the assumption of homogeneous chemical potentials.

2. First-order irreversible thermodynamics applied to intracellular processes

According to FOIT, after assuming the local equilibrium hypothesis, the entropy balance equation reads as follows [7]:

$$\rho\frac{ds}{dt} = -\nabla\cdot\vec{J}_s + \sigma, \tag{1}$$

where ρ is the mass density, s the system's specific entropy, $\vec{J}_s$ the entropy flow, and σ the entropy production rate. This equation means that the increments of entropy inside the system are due to within-produced entropy and to the entropy flow from the surroundings. The entropy flow and the entropy production rate are on their own given by

$$\vec{J}_s = \frac{1}{T}\left\{\vec{J}_q - \sum_k \mu_k\,\vec{J}_k\right\}, \tag{2}$$

and

$$\sigma = -\frac{1}{T^2}\vec{J}_q\cdot\nabla T - \frac{1}{T}\sum_k \vec{J}_k\cdot\left(T\nabla\frac{\mu_k}{T} - \vec{F}_k\right) - \frac{1}{T}\Pi\cdot\nabla\vec{v} - \frac{1}{T}\sum_j V_j A_j. \tag{3}$$

In these equations $\vec{v}$ is the baricentric velocity, $\vec{J}_q$ is the heat flow, $\vec{J}_k$ and μ_k are respectively the mass flow and the chemical potential corresponding to the k-th chemical species, $\vec{F}_k$ is the net external force acting per unit mass over the k-th component, Π is the viscous pressure tensor, V_j is the velocity of the j-th chemical reaction, and A_j its affinity. See Ref. 7. The total pressure tensor Λ is related to Π by $\Lambda = pI + \Pi$, with p the hydrostatic pressure, and I the identity tensor.

In studying intracellular processes, usage can be made of the former-mentioned assumptions about the homogeneity of p and T. It can also be supposed that the external force acting over any of the components is negligible. This has been claimed to be a reasonable assumption by Caplan and Essig [2] and Prigogine [3]. Therefore, Eq. (3) simplifies to

$$\sigma = -\frac{1}{T}\sum_k \vec{J}_k\cdot\nabla\mu_k - \frac{1}{T}\sum_j V_j A_j. \tag{4}$$

Equation (4) means that the most significant sources of entropy inside the cell are the chemical reactions and the mass flows driven by chemical potential gradients. If a steady state is attained, $ds/dt = 0$. This further implies that [see Eq. (1)]

$$\sigma = \nabla\cdot\vec{J}_s. \tag{5}$$

Equations (2), (4), and (5) imply that in steady state conditions, all the entropy produced inside the cell is dissipated as heat and/or as outward flows of highly entropic molecules, while the cell entropy remains constant.

The terms $-(1/T)V_jA_j$ in Eq. (4), related to chemical equations, can be positive or negative, depending on whether or not they correspond to spontaneous or non-spontaneous chemical reactions, respectively. On the other hand, the terms $-(1/T)\vec{J}_k\cdot\nabla\mu_k$ are always positive, since there are no forced mass-flows in the cytoplasm bulk.

3. Local definitions of "Power" and "Efficiency"

The second law of thermodynamics, in the formalism of FOIT, states that the entropy production rate must be non-negative point to point inside the cell. Therefore, from Eq. (4),

$$\sum_k \vec{J}_k\cdot\nabla\mu_k + \sum_j V_j A_j \le 0. \tag{6}$$

The chemical reactions velocities are scalar quantities driven by chemical affinities, which are scalar also. On the other hand, the mass flows $\vec{J}_k$ are vectorial quantities driven by vectorial chemical potential gradients. This means that chemical reactions are independent from flows $\vec{J}_k$ in the sense that the reaction velocities are not functions of $\nabla\mu_k$, and that flows $\vec{J}_k$ do not depend on the chemical affinities [3]. As a consequence of these facts, the flows $\vec{J}_k$ persist even when the chemical affinities are null and the chemical reactions stop, and *vice versa*. Therefore, both sums $\sum_k \vec{J}_k\cdot\nabla\mu_k$ and $\sum_j V_jA_j$ must be non-negative. *i.e.* the whole set of chemical reactions as well as the whole set of mass flows driven by chemical potential gradients are spontaneous processes which produce a positive amount of entropy. Given that inside the cell there are no mechanisms causing forced mass-flows, all the flows $\vec{J}_k$ are spontaneous, which means that $\vec{J}_k\cdot\nabla\mu_k \le 0$ for every k. Chemical reactions can be spontaneous or not depending on the sign of the affinities. Since the reaction velocities are positive or zero, a positive affinity means a non-spontaneous reaction and *vice versa*. Even though intracellular chemical reactions are in general related among them, not all of them are coupled to each other. Independent intracellular biochemical processes, formed by a finite set of coupled chemical reactions, can be identified. Their independence means that they are spontaneous by themselves. Then, we must have that

$$\sum_j A_j^{(i)}\,V_j^{(i)} \le 0, \tag{7}$$

for every independent biochemical process, indexed by i. The sum is extended in every case to the reactions involved in the corresponding process.

A special kind of intracellular biochemical processes are those known as energy-converting processes. At the microscopic level, those processes employ the energy stored in the

chemical bond of the reactants to produce the chemical bond of the reaction's products, which are important for the cell in the energetic and/or physiological senses. Despite most of the biological biochemical processes are quite complex and involve a great quantity of chemical reactions, in some special cases it is possible to see them as consisting of only a pair of global coupled reactions: a driving global spontaneous reaction that drives another global non-spontaneous reaction. For example, in the synthesis of ATP by aerobic glycolysis, the global driving reaction is the oxidation of glucose, while the driven reaction is the ATP synthesis itself. Given an independent energy converting biochemical process, for which the local equilibrium hypothesis is valid and the global driving and driven reactions can be identified, its entropy production rate σ_p, can be written from Eq. (4) as

$$\sigma_p = -\frac{1}{T}\left(A_1 V_1 + A_2 V_2\right). \tag{8}$$

Although such a process is only one of all the intracellular biochemical processes taking place inside the cell $\sigma_p \geq 0$, given its independence. This means that $A_1 V_1 + A_2 V_2 \leq 0$. In energy converting processes one of the reactions is spontaneous while the other is non-spontaneous. Therefore, one of the affinities is positive and the other negative. without loss of generality we can chose $A_1 \geq 0$ and V_1 to be the affinity and velocity of the driven non-spontaneous biochemical reaction and, $A_2 \leq 0$ and V_2 to be the affinity and velocity of the driving spontaneous biochemical reaction.

Under conditions of constant pressure and temperature, as we assume they are inside the cell, the affinity of any chemical reaction is nothing but the corresponding Gibbs free energy change ΔG, which is the amount of energy absorbed per mole of reaction advancement. $\Delta G \leq 0$ for spontaneous reactions and $\Delta G \geq 0$ for non-spontaneous reactions. Then, the absolute value of the product $A_i V_i$ measures the rate of energy absorbed or liberated by the i-th chemical reaction, depending on whether it is spontaneous or not, respectively. From this and the fact that $\sigma_p \geq 0$, an energetic interpretation to Eq. (8) is suggested. $-A_2 V_2$ is the volumetric rate of energy liberated by the spontaneous driving reaction, and $A_1 V_1$ is the volumetric rate of energy absorbed by the non-spontaneous driven reaction. A dissipation function Φ, measuring the rate of energy delivered by the driving reaction and not employed by the driven reaction, can then be defined as [2]

$$\Phi\left(\vec{r}\right) = T\sigma_p = -\left(A_1 V_1 + A_2 V_2\right). \tag{9}$$

The same arguments lead to define the rate of energy used by the driven non-spontaneous reaction (denoted by P and for economy called the power) as

$$P\left(\vec{r}\right) = A_1 V_1. \tag{10}$$

The efficiency of energy conversion (η) is defined by

$$\eta\left(\vec{r}\right) = -\frac{A_1 V_1}{A_2 V_2}. \tag{11}$$

The dependence of Φ, P, and η on the position $\vec{r}$ is emphasized in Eqs. (9)–(11) to remark the fact that those quantities are locally defined.

4. Global definitions of "Power" and "Efficiency"

The above given definitions of power and efficiency are impractical given the difficulty in measuring the affinities and the reaction velocities pointwise inside the cell. It is easier to measure these quantities as net values or averages. The net power of the non-spontaneous reaction inside the cell is

$$\hat{P} = \int_{\Omega} A_1\left(\vec{r}\right) V_1\left(\vec{r}\right) d^3 r, \tag{12}$$

with Ω the intracellular space. Let us make

$$A_1\left(\vec{r}\right) = \bar{A}_1 + \delta A_1\left(\vec{r}\right), \tag{13}$$

and

$$V_1\left(\vec{r}\right) = \bar{V}_1 + \delta V_1, \tag{14}$$

where $\bar{A}_1 = \left[\int_{\Omega} A_1\left(\vec{r}\right) d^3 r\right] / v\left(\Omega\right)$ is the average affinity and $\bar{V}_1 = \left[\int_{\Omega} V_1\left(\vec{r}\right) d^3 r\right] / v(\Omega)$ is the average velocity of the driven reaction. $v\left(\Omega\right)$ is the volume of the region Ω. From the definitions it follows that

$$\int_{\Omega} \delta A_1\left(\vec{r}\right) d^3 r = 0 \tag{15}$$

and

$$\int_{\Omega} \delta V_1\left(\vec{r}\right) d^3 r = 0. \tag{16}$$

By substitution of Eqs. (13)–(16) into Eq. (12) we get

$$\hat{P} = \bar{A}_1 \bar{V}_1 v\left(\Omega\right) + \int_{\Omega} \delta A_1\left(\vec{r}\right) \delta V_1\left(\vec{r}\right) d^3 r. \tag{17}$$

From Eqs. (15) and (16), the integral $\int_{\Omega} \delta A_1\left(\vec{r}\right) \delta V_1\left(\vec{r}\right) d^3 r$ can be identified with the spatial covariance of $\delta A_1\left(\vec{r}\right)$ and $\delta V_1\left(\vec{r}\right)$ [8]. Thus

$$\hat{P} = \bar{A}_1 \bar{V}_1 v\left(\Omega\right)\left[1 + \gamma \frac{\Delta_{A_1} \Delta_{V_1}}{\bar{A}_1 \bar{V}_1}\right]. \tag{18}$$

With γ the correlation coefficient between $\delta A_1\left(\vec{r}\right)$ and $\delta V_1\left(\vec{r}\right)$. Δ_{A_1} is the standard deviation of $\delta A_1\left(\vec{r}\right)$, and Δ_{V_1} is the standard deviation of $\delta V_1\left(\vec{r}\right)$. The correlation coefficient is by definition in the interval $[0, 1]$. On the other hand, despite the intracellular thermodynamic state is out of equilibrium, it is not very far from that state, as has being argued by several authors [2, 3, 6]. This in particular implies that the spatial fluctuations on the affinities and the reaction velocities are small, *i.e.* $\Delta_{A_1} / \bar{A}_1 \ll 1$ and $\Delta_{V_1} / \bar{V}_1 \ll 1$. From the above considerations it follows that

$$\hat{P} \approx \bar{A}_1 \hat{V}_1. \tag{19}$$

With $\hat{V}_1 = \bar{V}_1 v(\Omega)$ the net reaction velocity.

It can be shown analogously that $\int_\Omega A_2(\vec{r})\, V_2(\vec{r})\, d^3r \approx \bar{A}_2 \hat{V}_2$, from which a global efficiency can be defined as

$$\bar{\eta} \approx -\frac{\bar{A}_1 \hat{V}_1}{\bar{A}_2 \hat{V}_2}. \tag{20}$$

Equations (19) and (20) constitute definitions for the concepts of power and efficiency for intracellular energy converting biochemical processes. They are in agreement with the definitions introduced by Caplan and Essig [2] with a different formalism.

5. Concluding remarks

Definitions of power and efficiency for intracellular energy-converting biochemical processes have been introduced from the viewpoint of FOIT. These definitions are in agreement with those formerly introduced by Caplan and Essig [2], which have been successfully employed by some other authors to study the energetics of some biochemical reactions like ATP synthesis [9–11] and oxidative phosphorylation [5]. In the present work, the formalism of De Groot and Mazur [7] for FOIT was employed, rather than the formalism of Prigogine [3], which was used by Caplan and Essig. In the present approach all the assumptions are clearly stated as well as their physical meaning. One very strong restriction in the approach of Caplan and Essig is the assumption about the homogeneity of the chemical potentials. In the present approach, such assumption is not necessary.

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