Article

A Link between Nano- and Classical Thermodynamics: Dissipation Analysis (The Entropy Generation Approach in Nano-Thermodynamics)

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Abstract: The interest in designing nanosystems is continuously growing. Engineers apply a great number of optimization methods to design macroscopic systems. If these methods could be introduced into the design of small systems, a great improvement in nanotechnologies could be achieved. To do so, however, it is necessary to extend classical thermodynamic analysis to small systems, but irreversibility is also present in small systems, as the Loschmidt paradox highlighted. Here, the use of the recent improvement of the Gouy-Stodola theorem to complex systems (GSGL approach), based on the use of entropy generation, is suggested to obtain the extension of classical thermodynamics to nanothermodynamics. The result is a new approach to nanosystems which avoids the difficulties highlighted in the usual analysis of the small systems, such as the definition of temperature for nanosystems.

1. Introduction

In the last decades interest in engineering applications in composite materials, reacting systems, drug delivery and chemical storage has been continuously increasing. Small systems are ideal components for these uses because they present very high surface to volume ratios [1], but the consequences of the

progress in small system design and synthesis have pointed out the importance of scale-related properties, often different from the macroscopic ones [2].

But, what are the small systems? In this paper, small system means any system which has a size smaller than the range of the interactions of the forces acting on the system itself, so we consider several kinds of small systems [3,4]:

(1) Mesoscopic systems: Systems considered in the range size between the bulk materials and the molecules (of size of the order of 10^{-9}–10^{-6} m);

(2) Mesoscopically inhomogeneous systems: systems which have a mesoscopic length scale associated with spontaneous thermal fluctuations, so they are loose clusters, statistically appearing and disappearing with a definite lifetime;

(3) Soft condensed-matter materials: polymer solutions, polymer melts, microemulsions, foams, gels, colloidal dispersions, liquid crystals;

(4) Any system with long-range interactions.

Since the 19th century, thermodynamics has been developed to study the processes in macroscopic systems, which means that their number of particles are, at least, of the order of the Avogadro's number [5]. Since the 1930s, scientists and engineers have been trying to understand how to extend thermodynamic approaches and methods and the related fundamental quantities to small systems [3,6]: but, today, this remains an open problem. Indeed, in a general approach, the laws of thermodynamics operate at all scales, but at the small scale some phenomena, non visible at the macroscopic scale, must be taken into account; *i.e.*, the interfacial energy and thermal fluctuations [7–11]. As a result of these studies, many new approaches have been developed and improved, *i.e.*, non-equilibrium statistical thermodynamics, quantum thermodynamics, non-equilibrium fluids, molecular dynamics, *etc.* [12–22].

In this context, surface energies have been highlighted to modify the physical and chemical properties of small systems, which are taken into account by introducing a contribution to the total Gibbs free energy of the system [23–25].

On the other hand, applied and engineering thermodynamics is the science which studies both energy and its best use in relation to the available energy resources: energy and energy transformations, including power production, refrigeration and relationships among the properties of matter, including also living matter. The first law of thermodynamics expresses the conservation of the total energy, while the second law states that entropy continuously increases for the system and its environment [26]. Entropy can sometimes decrease within an open system, but only if it is used to increase entropy outside of the system. The second law highlights that energy has quality as well as quantity and any process occurs with a consequent decrease of this quality [26]. Consequently, the analysis of irreversibility in applied thermodynamics is a fundamental science for the analysis of open systems when energy transfers and energy transformations occur [27]. In this context, it has been highlighted that any effect in Nature is always the consequence of the dynamic balances of the interactions between the real systems and their environment [28–31]. Energy balances are the results of the exchange of energy between any real system and its environment. The real systems evolution is always related to the decrease of their free energy, in the least time [32–42].

Therefore, since 1993, a new approach to complex system has been developed [43–49] and improved [50–52] and recently applied to biological small systems [53–62] with particular regards to

the molecular motor analysis of V-ATPase [63]. It is based on the analysis of the interaction between systems and their environment by the use of the Gouy-Stodola theorem to evaluate the irreversibility and the dissipations in the interaction between systems and their environment, by considering entropy generation, which is related to the exergy lost by the systems during the interactions themselves [64–67].

Lastly, small systems sciences and engineering require an understanding of the small size behaviour of materials in order to use them in applications by modifying their physicochemical properties by controlling their size. In this context the thermal properties at the nanoscale represent a new opportunity of development for thermodynamics.

In this paper, just the Lucia and Grazzini developments and improvement of the Gouy-Stodola approach (GSGL-approach) to the analysis of irreversibility are suggested as a link between the classical and the small system approaches to thermodynamics. To do so, in Section 2 the usual approaches to nanosystems are summarized and discussed. In Section 3 a summary of the GSGL-approach is developed. Last, in Section 4, its application to small systems is proposed.

2. Nanothermodynamics: Considerations

A first approach to the thermodynamics of small systems can be obtained considering Hill's nanothermodynamics [15]. Hill began his analysis considering that the Gibbs, Euler and Gibbs-Duhem equations could be not valid when a small system doesn't satisfy the macroscopic limit:

$$\frac{N}{V} \underset{\substack{N \to \infty \\ V \to \infty}}{\to} n \tag{1}$$

where N is the number of particles of the system, V is the volume of the system and n is its number density, considered fixed and constant for any defined system, so he developed a theory to introduce the finite-size effects in the macroscopic thermodynamics. He obtained this result by introducing a new thermodynamic potential, named *subdivision potential U_S* [14], defined as:

$$U_S = \left(\frac{\partial U}{\partial N_S} \right)_{S,V,N} \tag{2}$$

where U is the internal energy, S is the entropy, V is the volume, N is the number of particles and N_S is the number of subdivisions, such that all these quantities are related to the whole system. This quantity disappears in the macroscopic approach to thermodynamics because the internal energy cannot have any variation if entropy, volume and the number of particles is constant:

$$dU = T\,dS - p\,dV + \mu\,dN \tag{3}$$

where T is the temperature, p is the pressure and μ is the chemical potential [68]. So, the pairs subdivision potential and number of subdivisions, (U_S, N_S), represent a new pair of conjugate thermodynamic variables.

In order to extend the classical thermodynamic approach to small systems, Hill introduced these quantities in the classical thermodynamic relations, considering that any composite system is macroscopic and that the small systems are non-interacting because their distance is larger than their interactions range. Consequently, for a small system, Euler's equation becomes:

$$\frac{U}{N_S} = T\frac{S}{N_S} - p\frac{V}{N_S} + \mu\frac{N}{N_S} + U_S \Rightarrow U_{ss} = TS_{ss} - pV_{ss} + \mu N_{ss} + U_S \tag{4}$$

and the Gibbs-Duhem equation becomes:

$$dU_S = -\frac{S}{N_S}dT + \frac{V}{N_S}dp - \frac{N}{N_S}d\mu \Rightarrow dU_S = -S_{ss}dT + V_{ss}dp - N_{ss}d\mu \tag{5}$$

where the suffix *ss* means small system. Consequently, the Gibbs' equation for the small systems is:

$$dU_{ss} = TdS_{ss} - pdV_{ss} + \mu dN_{ss} \tag{6}$$

the intensive parameter (T, p, μ) can be changed independently because of the variable size of small systems, which represents a new degree of freedom [14–19]. As a consequence of the subdivisions energy Equation (2) the entropy variation for subdivision, named subdivision entropy, can be introduced as:

$$S_S = -\frac{E_S}{T} = \left(\frac{\partial S}{\partial N_S}\right)_{U,V,N} \tag{7}$$

and it represents the entropy variation due to the ways of distributions of the particles in the small system. Consequently, the total entropy variation for a small system results:

$$S_{ss} = \frac{U_{ss}}{T} + \frac{p}{T}V_{ss} - \frac{\mu}{T}N_{ss} + S_S \tag{8}$$

So, as a consequence of the definition of:
  (1) Gibbs free energy [68]:

$$G = U - TS + pV \tag{9}$$

the chemical potential for a small system results as:

$$\mu_{ss} = \left(\frac{\partial G}{\partial N_{ss}}\right)_{T,p} = \mu + \frac{U_S}{N_{ss}} \tag{10}$$

  (2) Landau potential, named also grand potential [69]:

$$\Phi_G = U - TS - \mu N \tag{11}$$

the pressure for a small system results:

$$p_{ss} = -\left(\frac{\partial \Phi_G}{\partial V_{ss}}\right)_{T,p} = p - \frac{U_S}{N_{ss}} \tag{12}$$

so it follows that:

$$U_S = -TS_S = (\mu - \mu_{ss}) N_{ss} = (p - p_{ss}) V \tag{13}$$

But, in relation to Equations (2)–(13), two fundamental thermodynamic questions can be highlighted:

  (1) How is defined the temperature *T* for a small systems?
  (2) Is temperature the same for a composite system and for its components, the small systems?

So, to avoid these two conceptual difficulties, a new approach could be considered. The second law is one of the central and powerful laws of Nature. It is based on the concept of entropy [68]. On the other hand, entropy has always been a controversial topic. Indeed, during the 19th century, thermodynamics began its development as a physical science as a result of the studies of Sadi Carnot (1796–1832), Julius Robert von Mayer (1814–1878), Hermann Helmholtz (1821–1894), William Thomson (1824–1907) and Rudolf Clausius (1822–1888). But Helmholtz was the scientist who first determine the cultural profile of the thermodynamic researches [70–72]. Clausius, just developing the results of Helmholtz and Carnot, published the first formulation of the second law, as we know it today. Clausius suggested that heat is nothing more than a transformation of different kinds of energy, in which the total energy is a conserved quantity; indeed, he used the concept of ideal cycle of a reversible heat engine, as introduced by Carnot, in order to describe the work obtained by the transfer of heat from a reservoir at high temperature to one at low temperature. In 1851, Thomson obtained independently another formulation of the second law; he stated that it is impossible to create work by cooling down a thermal reservoir, so the fundamental nature of the second law results in a selection principle which can be expressed as an exclusion principle such that not all processes allowed by the energy conservation law may be realized during a real process [71]. Consequently, in order to study the evolution of real processes, Clausius first introduced in the 1850s–1860s a new quantity, the entropy S [73]. In 1871, Ludwig Boltzmann (1844–1906) introduced both the ergodic hypothesis, fundamental in statistical physics and in non-linear dynamics, and, in the next year, the H-theorem, which represents the first link between the second law and the statistical approach to entropy. Then, in 1889 Max Planck (1858–1947) highlighted the fundamental role of entropy and its statistical interpretation. Afterwords, Josiah Willard Gibbs (1839–1903) developed the ensemble approach and the entropy functional, highlighting the fundamental role of the maximum entropy approach in the analysis of the natural systems [71]. In 1909, Constantin Caratheodory (1873–1950) suggested an axiomatic formulation of the thermodynamics based on the pfaffian differential forms [74], but in 1929, Walter Schottky (1886–1976) was the first to extend the approach to thermodynamics for industrial applications [71]. Recently, just the thermodynamic formalism and the related links between macroscopic and microscopic approach to entropy have come to clearly play an important role in nonlinear sciences and complex systems with particular regards to power engineering, environmental sciences, quantum theory, low temperature physics, large scale and small scale physics, biophysics, biochemistry and biomedicine, information sciences, *etc.*. The first scientist who was interested in the relation between observer and object, information and entropy was James Clerck Maxwell (1831–1879). Then this topic was developed by Leo Szilard (1898–1964), John von Neumann (1903–1957), Garrett Birkhoff (1911–1996) and Edwin Thompson Jaynes (1922–1998), obtaining the link between the foundations of statistical physics with the information theory by using the maximum entropy principle which states that the probability distribution is selected such that the uncertainty remains largest in relation to the constraints.

Every macroscopic equilibrium state of a system, named macrostate, is compatible with a great number of microscopic states, named microstates. The relation between the macro- and microscopic thermodynamic descriptions of the (macro)state is based on the probability of occupation of microstates. In this context the observed values of any physical quantity results as the average values over the distribution of microstates.

Entropy is a concept that it is not usually easy to understand, so in relation to the approach used many different definitions of entropy have been introduced [75]. In order to avoid the increase of the number

of the entropy functions, a generalized Boltzmann-Gibbs entropy has been introduced and the entropy definition was suggested as [20–22]:

$$S_q = \frac{k}{1-q}\left(\sum_{i=1}^{\Omega} p_i^q - 1\right) = k \ln_q \Omega \tag{14}$$

where Ω is the total number of microstates, p_i is the probability of finding the system in the *i*-th microstate, q, named entropic index, is a parameter which characterizes the degree of nonextensivity of the entropy for non completely accessible systems, such that, for a conserved energy system:

$$S_q(A+B) = S_q(A) + S_q(B) + \frac{1-q}{k} S_q(A) S_q(B)$$
$$\sum_{i=1}^{\Omega} p_i^q = \Omega^{1-q} \tag{15}$$

and k is a constant such that:

$$k = k_B \quad \text{if } q = 1$$
$$k \neq k_B \quad \text{if } q \neq 1 \tag{16}$$

where k_B is the Boltzmann's constant and $\ln_q \xi$ is the *q*-logarithm, defined as:

$$\ln_q \xi = \frac{\xi^{1-q} - 1}{1-q} \tag{17}$$

The Hill approach can be developed in term of Tsallis nonexstensive formalis by defining the subdivision potential Equation (2) as:

$$U_S = TS_q - \frac{kT}{1-q} \Sigma_q \ln \Sigma_q$$
$$\Sigma_q = \sum_{i=1}^{\Omega} p_i^q \tag{18}$$

and considering the following relations [20–22]:

$$dS_q = \frac{1}{T} dU + \frac{p}{T} dV - \frac{\mu}{T} dN$$
$$\frac{\Sigma_q \ln \Sigma_q}{1-q} = \frac{U}{T} + \frac{pV}{T} - \frac{\mu N}{T}$$
$$\frac{\ln \Sigma_q}{k} dS_q = U\, d\left(\frac{1}{T}\right) + V\, d\left(\frac{p}{T}\right) - N\, d\left(\frac{\mu}{T}\right) \tag{19}$$

But, again in relation to Equation (19), the previous two thermodynamic questions remain open:

(1) How is defined the temperature *T* for a small systems?
(2) Is temperature the same for a composite system and for its components, the small systems?

In relation to small systems, the concept of variance of the distribution and fluctuations are fundamental to develop a thermodynamic approach. Indeed, the energy of any system fluctuates around its average value, without representing the beginning of a process or a transition, but only the dynamic character of any thermodynamic configuration [76–78]. In the macroscopic limit Equation (1)

fluctuations can be neglected, while in nanoscale systems they must be taken into account because a lot of nonascole thermal properties [79] and the transport phenomena [57–61,64] can be evaluated just by also using the fluctuation theory. The fluctuation of a physical quantity ξ can be mathematically defined as the deviation $\delta\xi$ of any single measurement of ξ from its average value $\langle\xi\rangle$:

$$\delta\xi = \xi - \langle\xi\rangle \tag{20}$$

The relevance of the fluctuation can be evaluated considering its fractional deviation:

$$\sigma_{\xi r} = \frac{\sigma_\xi}{\langle\xi\rangle} \tag{21}$$

where σ_ξ is the standard deviation of ξ:

$$\sigma_\xi = \sqrt{\left(\xi - \langle\xi\rangle\right)^2} \tag{22}$$

The probability of observing a microstate characterized by the physical quantity ξ is proportional to its multiplicity:

$$p(\xi) \propto \Omega(\xi) \tag{23}$$

and the related power expansion for the Boltzmann's entropy around the equilibrium state ξ_{eq} results:

$$S = k_B \ln\Omega(\xi) = S_{eq} + \left(\frac{\partial S}{\partial\xi}\right)_{eq}(\xi - \xi_{eq}) + \frac{1}{2}\left(\frac{\partial^2 S}{\partial\xi^2}\right)_{eq}(\xi - \xi_{eq})^2 + o\left((\xi - \xi_{eq})^2\right) \tag{24}$$

But if the system is isolated, the relation Equation (24) becomes:

$$S - S_{eq} \approx \frac{1}{2}\left(\frac{\partial^2 S}{\partial\xi^2}\right)_{eq}(\xi - \xi_{eq})^2 \tag{25}$$

consequently, considering the Boltzmann definition of entropy, the probability distribution results:

$$p(\xi) = \frac{\exp\left[\frac{1}{2}\left(\frac{\partial^2 S}{\partial\xi^2}\right)_{eq}(\xi - \xi_{eq})^2\right]}{\int_{-\infty}^{\infty} \exp\left[\frac{1}{2}\left(\frac{\partial^2 S}{\partial\xi^2}\right)_{eq}(\xi - \xi_{eq})^2\right]d\xi} \tag{26}$$

and the variance of the physical quantity results [78]:

$$\sigma_\xi^2 = \frac{\int_{\langle\xi\rangle}^{\infty} \exp\left[\frac{1}{2}\left(\frac{\partial^2 S}{\partial\xi^2}\right)_{eq}(\xi - \xi_{eq})^2\right]}{\int_{-\infty}^{\infty} \exp\left[\frac{1}{2}\left(\frac{\partial^2 S}{\partial\xi^2}\right)_{eq}(\xi - \xi_{eq})^2\right]d\xi} = -\frac{k_B}{\left(\frac{\partial^2 S}{\partial\xi^2}\right)_{eq}} \propto \frac{1}{\sqrt{N}} \geq 0 \tag{27}$$

Therefore, at the macroscopic limit the fluctuations are so small as to be neglected. This approach, developed by Einstein, can be used also for non-isolated systems, for which we consider the stationary states [80], so fluctuations represent also a fundamental bases in non-equilibrium thermodynamics.

In relation to fluctuation Brownian motion must also be considered. It always exists just as a fluctuation, related both to thermal molecular motion inside the system and to dissipation for interaction between system and external forces. In this context of internal and external irreversibility, Ehrenfest's fundamental question on the existence of a functional which achieves its extreme value, as entropy does for the stationary states in equilibrium thermodynamics, must be considered, so many fluctuation theorems have been developed to obtain this general principle of analysis and design of the stationary systems for complex, and in this context, also small systems [81–90]. Strictly related to this topic, is the analysis of self-organizing systems introduced by Mayer, Boltzmann, Erwin Schrödinger (1887–1961) and Ilya Prigogine (1917–2003). The basis of their approach is the fundamental role of the exchanges between the system and the surroundings. Related to this topic, the development of non-equilibrium or irreversible thermodynamics, begun by Joseph John Thomson (1856–1940), John William Strutt Rayleigh (1842–1919), Pierre Maurice Marie Duhem (1861–1916), Władysław Natanson (1864–1937), Gustav Jaumann (1863–1924) and formalized by Louis Georges Gouy (1854–1926), Aurel Stodola (1859–1942), Lars Onsager (1903–1976), Carl Henry Eckart (1902–1973), Josef Meixner (1908–1994), Hendrik Casimir (1909–2000), Prigogine and Sybren Ruurds De Groot (1916–1994) it must be considered too. Indeed, the analysis of irreversible processes is essential in the study of non-linear sciences, which need a non-linear dynamical approach. Thermodynamics is just a theory of the collective behaviour of complex systems from engines to biological structures, from transport phenomena to black holes, *etc.*, and all these phenomena obey the second law. To develop this law for small systems a mechanical formulation is required [91], but, to do so, the surface effects must be taken into account [92]. They can be classified in two general sets [25]:

(1) Smooth size effects: the physical quantities vary monotonically with the system size so that a scaling law can be introduced to describe the bulk behaviour;
(2) Specific size effects: the physical quantities don't vary monotonically with the system size so no scaling law can be introduced and, seldomly, some size properties are unique for the finite system considered;

and they represent the nanosystems property of the high surface to volume ratio increase with size decrease. This effect can be taken into account by introducing a size energy component in the total Gibbs free energy of the systems [23]. Recently, classical thermodynamics has been highlighted to represent a fundamental approach to describe the nanosystems behaviours in relation to their surface properties [95], even if it remains fundamental a link between macroscopic and microscopic formulation [96], so that the Equation (3) becomes:

$$dU = TdS - pdV + \mu dN + \gamma \, dA_I \tag{28}$$

where A_I is the interfacial surface and γ is the interfacial free energy [97].

3. GSGL-Approach: Fundamentals

In the previous Section some considerations on nanothermodynamics have been developed. Some open questions were highlighted:

(1) How is the temperature T defined for a small system?
(2) Is temperature the same for a composite system and for its components, the small systems?
(3) Which is the right statistics for small systems?

These are important questions and they lead to new improvements to thermodynamics, but in order to use classical thermodynamics in small systems analysis, it could be useful to consider the classical analysis of irreversibility as recently developed by using the Gouy-Stodola approach [53].

Entropy was introduced in classical thermodynamics in relation to the equilibrium states and reversible transformations. It is a state function. When an irreversible system is considered [98,99], mathematical inequalities appear, so, entropy generation was introduced just to avoid them. Consequently, the second law defines the entropy variation, ΔS, for an irreversible system, as [53]:

$$\Delta S = \int \left(\frac{\delta Q}{T} \right)_{rev} = \Delta S_e + S_g \tag{29}$$

where ΔS is the real entropy variation, ΔS_e is the reversible entropy variation and S_g is the entropy generation, *i.e.*, the entropy variation due to irreversibility. But, during any process, only entropy really varies, so nothing is really *produced* or *generated* [53]. Consequently, entropy generation, the entropy variation due to irreversibility, S_g, is not more than a quantity that allows us to measure how far the system is from the state that the system could attain through a reversible path. The analytical definition of entropy generation is defined as [5]:

$$S_g = \int_0^\tau \dot{S}_g dt \tag{30}$$

where τ is the lifetime of the process under consideration, which can be defined as the range of time in which the process occurs [5,53]:

$$\dot{S}_g = \frac{dS}{dt} - \sum_{i=1}^n \frac{\dot{Q}_i}{T_i} - \sum_{in} G_{in} s_{in} + \sum_{out} G_{out} s_{out} \tag{31}$$

where Q is the heat exchanged, T is the temperature of the thermal source, s is the specific entropy and G is the mass flow. Considering the results obtained in non equilibrium thermodynamics [100] the entropy generation results:

$$S_g = \int_V \left(-\int_o^{\tau_1} \frac{v}{T^2} \mathbf{J}_q \cdot \nabla T dt - \int_o^{\tau_2} v \sum_k \mathbf{J}_k \cdot \nabla \left(\frac{\mu_k}{T} \right) dt - \int_0^{\tau_3} \frac{v}{T} \mathbf{\Pi} : \nabla \dot{\mathbf{x}}_B dt - \int_0^{\tau_4} \frac{v}{T} \sum_j J_j \mathcal{A}_j + \int_0^{\tau_5} \frac{v}{T} \sum_k \mathbf{J}_k \cdot \mathbf{F}_k \right) dV =$$
$$= S_{g,tf} + S_{g,dc} + S_{g,vg} + S_{g,cr} + S_{g,de} \tag{32}$$

where [57–61,63]:

(1) $S_{g,tf}$ is the entropy generation due to the thermal flux driven by temperature difference;

(2) $S_{g,dc}$ is the entropy generation due to the diffusion current driven by chemical potential gradients;

(3) $S_{g,vg}$ is the entropy generation due to the velocity gradient coupled with viscous stress;

(4) $S_{g,cr}$ is the entropy generation due to the chemical reaction rate driven by affinity, always positive [42–44];

(5) $S_{g,de}$ is the entropy generation due to the dissipation due to work by interaction with the environment;

(6) $\mathbf{II} = \mathbf{P} - p\,\mathbf{I}$ with $\mathbf{P}$ total pressure tensor, p hydrostatic pressure and $\mathbf{I}$ identity matrix of which the elements are $I_{jk} = \delta_{jk} = 1$ if $j = k$ and 0 in the other cases, $\mathbf{a} : \mathbf{b} = \sum_{ij} a_{ij} b_{ji}$ is the product between two tensors $\mathbf{a}$ and $\mathbf{b}$;

(7) $\mathbf{J}_k = \rho_k \left(\dot{\mathbf{x}}_k - \dot{\mathbf{x}}_B \right)$ is the diffusion flows and $\mathbf{F}_k$ are the forces;

(8) J_j is the chemical reaction rate of the j-th chemical reaction and v_{ij} are quantities such that if they are divided by the molecular mass of the i-th component they are proportional to the stoichiometric coefficients, $A_j = \Sigma_k\, v_k\mu_{jj}$, the chemical affinity;

(9) μ_i are the chemical potentials;

(10) $d/dt = \partial/\partial t + \dot{\mathbf{x}}_B \cdot \nabla$;

(11) $\mathbf{J}_q$ is the heat flow, $\dot{\mathbf{x}}_i$ is the relative velocity in relation to the centre of mass reference, and $\dot{\mathbf{x}}_B$ is the centre of mass velocity;

(12) s is the specific entropy, u is the internal specific energy, v is the specific volume,

(13) T is the temperature;

and τ_i, $i \in [1,5]$, are the lifetimes [53] of any process and the relation is considered in the time $\tau = \max\{\tau_i\}$ It must be highlighted that any work related to electric fields inside or on the boundaries of the systems can be expressed by variation of the affinities of the ions involved, so that any work for internal electric fields is taken into account in the term $S_{g,cr}$.

Now, we have obtained a general analytical expression of the entropy generation. In order to use this quantity in the analysis of the complex systems steady states, it is interesting to understand its physical-mathematical behaviour for stationary states. To do so, a real system is considered. For such a system, the theorem of kinetic energy can be written as [53]:

$$W_{es} + W_{fe} + W_i = \Delta E_k \tag{33}$$

where W_{es} is the work done by the environment on the system, *i.e.*, the work done by the external forces to the border of the system, W_{fe} is the work lost due to external irreversibility, E_k is the kinetic energy of the system, W_i is the work of the internal forces on the border of the system, named internal work, such that [53]:

$$W_i = W_i^{rev} - W_{fi} \tag{34}$$

with W_i^{rev} reversible internal work and W_{fi} work lost due to internal irreversibility. Moreover, the following relation must be taken in account [53]:

$$W_{se} = -W_{es} - W_{fe} \tag{35}$$

where W_{se} is the work done by the system on the environment, *i.e.*, the work done from the internal forces to the border of the system. Consequently, the following formulation of the first principle can be obtained [53]:

$$Q - W_{se} = \Delta U + \Delta E_k \tag{36}$$

with U the internal energy of the system.

In relation to these last equations, it must be highlighted that the system cannot use all the energy inflow, so we must take into account the available energy of the system, named exergy, B, *i.e.*, the maximum work that could be done by a system. It is related to a reference environment, assumed to be infinite, at equilibrium, and to enclose all other systems. This environment has a well known temperature, pressure and chemical composition [5], so exergy allows us to measure the potential of the system or flow to cause changes [5], because it is a non-equilibrium system in relation to the reference environment. Introducing the exergy lost for irreversibility and dissipation, B_λ, it is possible to prove the Gouy-Stodola theorem [5,53]:

$$B_\lambda = \int_0^\tau \left(\dot{B}_W^{rev} - \dot{B}_W \right) dt = W_\lambda = T_0 S_g \tag{37}$$

Now, considering the relations Equations (33)–(35), the work lost due to external irreversibility can be written in relation to the Gouy-Stodola theorem as [4,53]:

$$W_{fe} = T_0 S_g \tag{38}$$

where T_0 is the environmental temperature and S_g is the entropy generation. Consequently, always considering the relations Equations (33)–(35), the link between the internal and the external work lost due to irreversibility can be easily obtained [53]:

$$W_{fi} - W_{fe} = W_i^{rev} + W_{es} - \Delta E_k \Rightarrow W_{fi} - T_0 S_g = W_i^{rev} + W_{es} - \Delta E_k \tag{39}$$

But, another expression of the work lost can be written as [53]:

$$\begin{cases} W_\lambda = \int_V \left(\int_0^\tau dt Tv\sigma - \phi \right) dV = (T - T_0) S_g \\ W_\lambda = W_{fi} - T_0 S_g \end{cases} \tag{40}$$

where $\sigma = \delta^2 S_g / dt dV$ is the entropy production density, φ is the dissipation function, v is the specific volume, τ is the lifetime of the process and V is the control volume of the system, the internal irreversibility can be easily obtained as [5]:

$$W_{fi} = \int_V \int_0^\tau dt Tv\sigma dV = TS_g \tag{41}$$

which is the analytical expression for the work lost for internal dissipation.

All the results obtained in the analysis of the processes which occur in open systems are based on the common principle of the least time. This principle hold to the optimal paths approach which is nothing more than a redistribution energy approach.

Now, considering the effect of the potential energies variation can be evaluated as [53]:

$$\sum_{j=1}^{N}\Delta E_{pj} = W_i + W_{es} \tag{42}$$

where E_{pj}, $j = 1,...,N$, are the potential energies, W_i the internal work, and W_{es} the work done by the external forces to the border of the system, and considering also that:

$$\delta W_{es} + \delta W_{fe} + \delta W_i = dE_k \tag{43}$$

it is possible to introduce the thermodynamic Lagrangian as [53]:

$$d\mathcal{L} = dE_k - \sum_{j=1}^{N}dE_{pj} = dE_k - (\delta W_i + \delta W_{es}) = \delta W_{fe} = \delta W_{\lambda} \Rightarrow \mathcal{L} = W_{fe} = -T_0 S_g \tag{44}$$

and the related action as:

$$\mathcal{A} = \int_0^{\tau} dt\mathcal{L} = -T_0 \int_0^{\tau} dtS_g \tag{45}$$

where τ is the lifetime of the process, as previously introduced. As a consequence of the least time approach, it follows:

$$\delta\mathcal{A} \leq 0 \Rightarrow \delta S_g \geq 0 \tag{46}$$

if it is considered from the environment and:

$$\delta\mathcal{A} \leq 0 \Rightarrow \delta S_g \leq 0 \tag{47}$$

if it is considered from the inside of the system, so the entropy generation results maximum if it is evaluated from the environment and minimum if it is evaluated from the inside of the system [53].

Therefore, the entropy generation results always in an *extremum* at the stationary states. Moreover, the change in energy always causes a transition between two different thermodynamic states, and it always results in a path-dependent processes, so these flow of quanta in a process is nothing more than a flow of exergy, which causes the specific entropy generation rate [53]:

$$\dot{s}_g = \mathbf{J}_U \cdot \nabla\left(\frac{1}{T}\right) + \sum_i \mathbf{J}_{N_i} \cdot \nabla\left(\frac{\mu}{T}\right) \tag{48}$$

where $\mathbf{J}_U$ is the energy flow, T is temperature, μ is the chemical potential, and $\mathbf{J}_{Ni}$ is the molar flow, it follows that:

$$
\begin{aligned}
(T-T_0)\dot{s}_g &= (T-T_0)\left[\mathbf{J}_U \cdot \nabla\left(\frac{1}{T}\right) + \sum_i \mathbf{J}_{N_i} \cdot \nabla\left(\frac{\mu}{T}\right)\right] = \\
&= T\left(1-\frac{T_0}{T}\right)\mathbf{J}_U \cdot \nabla\left(\frac{1}{T}\right) + T\sum_i\left(1-\frac{T_0}{T}\right)\mathbf{J}_{N_i} \cdot \nabla\left(\frac{\mu}{T}\right) = \\
&= T\mathbf{J}_B \cdot \nabla\left(\frac{1}{T}\right) + T\dot{s}_g^{ch}
\end{aligned}
\tag{49}
$$

where $\mathbf{J}_B$ is the exergy flow density and $\dot{s}_g^{ch}$ is the chemical component of the entropy generation density rate. This relation, integrated in time and volume, holds:

$$W_\lambda = W_{fi} - W_{fe} = (T - T_0) S_g =$$

$$= T \int_0^\tau d\tau \int_V dV \left[\mathbf{J}_B \cdot \nabla\left(\frac{1}{T}\right) + \dot{s}_g^{ch} \right] \Biggr\} \Rightarrow W_i^{rev} + W_{es} - \Delta E_k = T \int_0^\tau d\tau \int_V dV \mathbf{J}_B \cdot \nabla\left(\frac{1}{T}\right) + T S_g^{ch}$$

$$W_\lambda = W_{fi} - W_{fe} = W_i^{rev} + W_{es} - \Delta E_k \Biggr\}$$

(50)

In this relation it is possible to evince that the system reacts to the external forces by exergy flows, which evolves in the least time, so [83]:

$$S_g \leq T_0 \frac{T_1 - T_0}{T - T_0} W_{\lambda 1} \quad \forall T \neq T_0$$

(51)

where $W_{\lambda 1}$ is the lost work required to maintain the state 1 at the temperature $T_1 \neq T_0$, in agreement with the previous result Equation (46).

These results are also related to the Carnot efficiency. Indeed, considering an ideal system which absorbs the heat Q_1 from the thermostat at temperature T_1, it follows:

$$S_g \leq Q_1 \frac{1}{T_1}$$

(52)

This relation was highlighted to be the entropy variation required to maintain the process [53], so considering the second thermostat at temperature T_2 of a cycle, the heat not converted in useful work becomes:

$$Q_2 = T_2 S_g = Q_1 \frac{T_2}{T_1}$$

(53)

and the maximum work done by a system operating on a Carnot's cycle results:

$$W = Q_1 - T_2 S_g = Q_1 \left(1 - \frac{T_2}{T_1} \right)$$

(54)

which is just the well known Carnot efficiency:

$$\eta = \frac{W}{Q_1} = 1 - \frac{T_2}{T_1}$$

(55)

Consequently, the entropy generation can be considered as an "exergy footprint Δ" in the environment, due to the processes occurring inside the complex system: information lost by the system and gained by the environment. This exergy footprint can be defined as the exergy difference in a cyclic transformation by using Noether's theorem [34]:

$$2 \int_0^\tau E_k dt = nh \quad \text{with} \quad n \geq 1$$

(56)

with n multiples of quanta and h Planck's constant. By using the previous relations, it follows that [53]:

$$\left(W_i^{rev} + W_{es} \right) \tau = n\pi\hbar + T_0 \tau S_g$$

(57)

and, considering that the entropy generation is always positive for any real process or null for an ideal reversible process, the consequent entropy generation results:

$$S_g = \frac{\Delta}{T_0} \tag{58}$$

with T_0 a reference temperature, which can be considered the temperature of the environment in contact with the system.

4. GSGL-Approach and Small Systems

In the last decades, molecular machines have highly been studied [101,102] and their use has been suggested both in industrial nanotechnology and in medicine. In this Section an example of application of the GSGL approach to small systems is proposed. The small system considered is a molecular machine, namely V-ATPase.

The environment of a small system can be considered as a thermostat, so it has a constant temperature T_0, so the environment of a small system behaves as a thermostat. As a consequence of the previous considerations, we suggest to introduce the irreversible term in the Boltzmann's definition of the entropy as follows [103]:

$$\Delta S = k_B \ln \frac{\Omega_2}{\Omega_1} + S_g \tag{59}$$

where S_g is evaluated by considering the relation Equation (32), equivalent to the relation Equation (58), and ΔS is the entropy variation between two stationary states 1 e 2 such that:

$$\begin{aligned} S_1 &= k_B \ln \Omega_1 \\ S_2 &= k_B \ln \Omega_2 \end{aligned} \tag{60}$$

and S_g is consequent to the irreversibility during the transition (process). This new expression for the entropy variation is completely time-irreversible for any real process: it could represent a new approach to solve the Loschmidt paradox. It is obtained by analysing the interactions of the system in relation to its environment (a thermostat).

Now, we consider an example of application. The basis of metabolism energy conversion consists in the generation and the hydrolysis of ATP, which occurs across a trans-membrane electromotive gradient. This energy conversion can be obtained by transitioning the electrochemical energy into the chemical energy of the terminal phosphoric anhydride bond of the ATP. This can occur by the action of an enzyme, which works as a proton-pumping ATP synthetase. A mechanochemical model for the V-ATPase was suggested by Grabe, Wang, and Oster [104] and it is based on the hypothesis that ATP concentrations are sufficiently high so that hydrolysis is not rate limiting. The V-ATPase structure is composed of a counter-rotating stator and a rotor. This accepted model for the active transmembrane ion transport is the alternating access mechanism. Ions are bound tightly on the low concentration side of the membrane. A conformational change weakens their binding affinity by exposing them to the high concentration side; as a consequence, they dissociate. Then, the pump changes its conformation in order to begin the cycle again.

V-APTase hydrolyses ATP to obtain the required energy for its work. The fundamental reaction is:

$$\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P} \tag{61}$$

and, consequently, a H^+ ion is pumped into the cell:

$$H^+_{out} \xrightarrow{\quad H^+_{memb} \quad} H^+_{in} \tag{62}$$
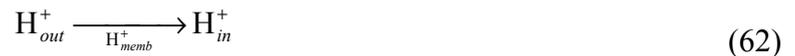
where *out* means outside, *in* refers to inside and *memb* stands for across the membrane.

The efficiency of V-ATPase can be evaluated as [102]:

$$\eta = \chi \frac{\Delta G_P}{\Delta G_{ATP}} \tag{63}$$

where ΔG_{ATP} is the free energy variation due to the hydrolysis of a single ATP molecule (~50 kJ·mol^{-1}), χ is the coupling ratio ($\chi = J_H/J_{ATP}$, being J_H the proton flux and J_{ATP} the ATP hydrolysis rate) and ΔG_P is the free energy variation required to move the proton across the membrane [106]:

$$\Delta G_P = \Delta\phi - 2.3 \frac{RT_0}{F} \Delta pH \tag{64}$$

where $\Delta\phi$ is the membrane potential, R is the gas constant (8.314 J mol^{-1}K^{-1}), F is the Faraday constant (96.485 × 10^3 A·s·mol^{-1}), and 2.3 ΔpH is the physiological concentration gradient. The coupling ratio χ is affected both by the pH gradients and by the membrane potential. So, the work dissipated in wasted heat yields:

$$W_\lambda = T_0 S_g = (1-\eta)\Delta G_{ATP} = \Delta G_{ATP} - \frac{J_H}{J_{AATP}}\left(\Delta\phi - 2.3\frac{RT_0}{F}\Delta pH\right) \tag{65}$$

and the entropy generation is easily evaluated as:

$$S_g = \frac{\Delta G_{ATP}}{T_0} - \frac{J_H}{J_{AATP}}\left(\frac{\Delta\phi}{T_0} - 2.3\frac{R}{F}\Delta pH\right) \tag{66}$$

This example highlights how entropy generation allows us to link between the microscopic (flows, pH, *etc.*) and the macroscopic thermodynamic quantities (efficiency, heat, *etc.*). Therefore, all the optimization methods usually used in engineering thermodynamics and based on the use of entropy generation can be introduced in the analysis and design of small systems in relation to the application aims. In particular, in relation to Equation (66), it follows that it is possible to control the proton fluxes across the cell membrane by controlling the electric field of the membrane or the pH in the cell environment.

5. Conclusions

The interest in designing nanosystems is growing [107]. In particular, mechanical engineering uses a great number of optimization approaches to design macroscopic machines. If these methods could be introduced in the design of small systems it would represent a great improvement in nanotechnologies, but to do so, it is necessary to extend classical thermodynamic analysis to small systems.

In this paper the GSGL approach is suggested to achieve this result. Indeed, this approach is based on the use of entropy generation, the variation of entropy related to irreversibility. Irreversibility is present also in small systems, as the Loschmidt paradox highlighted. Here a solution to this paradox is introduced to extend the use of the entropy generation to small systems thus obtaining a link between local and global thermodynamic quantities. Moreover, the use of this new approach avoids the difficulties

highlighted in the usual analysis of the small systems, such as the definition of a temperature for nanosystems, even if some thermodynamicists have began the analysis of this topic [93,94,105,108]. Moreover, in this paper we have only introduced a first application of the GSGL approach to nanosystems. This approach will be improved in relation to the other theories not yet analyzed. This choice has been done in relation to the following considerations:

(1) The fundamental aim of this paper: to suggest a link between engineering thermodynamics and nanosystems in order to employ a first approximation use of the usual engineering design of machines in designing molecular machines for medical applications. However, engineering thermodynamics is related to the classical approach to thermodynamics. Consequently, in this paper, some fundamental approaches [109] have not been considered. Indeed, these new and original approaches doesn't have a clear link with engineering thermodynamics, so in order to develop the GSGL approach to them, it is necessary to obtain this link;

(2) The proposed approach hasn't developed the size effects because they have just been discussed in depth in some recent papers [110].

Conflicts of Interest

The author declares no conflict of interest.

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