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Review Article

Different Thermodynamic Theories and Different Heat Conduction Laws[*]

Vito Antonio Cimmelli
Department of Mathematics and Computer Science, University of Basilicata,
85100 Potenza, Italy
e-mail: vito.cimmelli@unibas.it

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Berlin, Germany

Abstract

We present an overview of the modern approaches to continuum nonequilibrium thermodynamics from the perspective of their connection with the problem of heat conduction with finite speed. The celebrated Cattaneo and Guyer–Krumhansl equations for the evolution of the heat flux are reinspected in the framework of the different thermodynamic theories which, in such a way, are reviewed and compared.

1.   Preface

In this paper we provide an overview of the modern approaches to continuum non-equilibrium thermodynamics, and of their connection with the problem of heat conduction with finite speed of propagation. Indeed, all modern thermodynamic theories stem from a precise point of view on the problem of heat conduction. On this subject, the celebrated paper by Cattaneo [1], where it is observed that the classical heat equation leads to the "paradox" of infinite speeds of propagation of the thermal disturbances, stimulated several researches into different directions. We can classify these researches in two different categories: the conservative approaches and the nonconservative

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[*] *In memory of Antonio Mario Tamburro, Rector Magnificus of the University of Basilicata*

ones. The first type of approach is due to those scientists who wanted to conserve the general schemes of the existing thermodynamic theories, such as classical irreversible thermodynamics and rational thermodynamics, and tried to describe hyperbolic heat conduction in the realm of these theories. The nonconservative approaches are those that considered the classical theories much too general to include a satisfactory treatment of the heat conduction with finite speed of propagation, and postulated some further requirements. Hence, new theories have been formulated and new schools of thermodynamics have been founded in the last decades [2, 3]. This fact should be regarded positively, since the building up of new theories has stimulated several discussions and comparisons of different approaches. This is one of the reasons why modern non-equilibrium continuum thermodynamics is so fascinating today and so attractive for scientists.

Although Cattaneo was not a thermodynamicist, "paradoxically" he contributed a lot to the development of modern thermodynamics, because his paper stimulated the formulation of new theories.

Today the importance of this paper is much more related to the history of thermodynamics rather than to the results contained therein. Indeed, a more sophisticated analysis of Cattaneo conclusions, developed by G. Fichera [4] and W. A. Day [5, 6], proved that the celebrated Cattaneo paradox actually is not a paradox and that also in Fourier heat conduction theory one can get finite speeds. Notwithstanding, its influence on non-equilibrium thermodynamics was enormous and positive beyond any doubt.

Furthermore, if we look at the different schools with more attention, we discover that these are not so far apart as might appear at the first sight, since several connections emerge.

The aim of this presentation is to point out the differences and the similarities between the thermodynamic theories.

In Section 2 we provide a sketch of the Fourier heat conduction theory leading to the so-called Cattaneo paradox. The experimental conditions under which the theory is developed, and which should be taken into account in evaluating the speed of propagation of thermal disturbances, are pointed out.

In Section 3 we summarize the main features of heat conduction at low temperatures. The equations introduced by Cattaneo [1] and by Guyer–Krumhansl [7, 8], describing, respectively, the hyperbolic and parabolic regimes, are presented. From the microscopic point of view the aforementioned regimes are related to the so called phonon gas hydrodynamics, which determines the

behavior of some characteristic material functions such as heat conductivity and relaxation times.

In Section 4 we analyze how the problem of finite wave speeds (second sound propagation) is solved in the framework of rational thermodynamics [9, 10][1]. This task can be achieved by using the theory of internal state variables, either in the local or in the gradient approach. A new dynamic temperature, which is capable of propagating with finite speed, is introduced as an internal variable. The related initial and boundary value problem is considered and typical numerical solutions are presented.

In Section 5 the propagation of heat waves is modelled according to the basic postulates of rational extended thermodynamics [11][2]. The 4-fields and 9-fields models, both ruled by a system of balance equations following the kinetic theory, are presented. We show that both systems are capable of describing second sound at different levels of approximation.

In Section 6 we prove that, under suitable constitutive assumptions, classical irreversible thermodynamics [14, 15][3] yields both the 4-fields and 9-fields systems and also the Guyer–Krumhansl equation.

In Section 7 such an equation is studied in detail. It is shown that it is compatible with the extended theories provided one assumes that the constitutive functions depend on the gradients of the unknown fields. Two models are presented. The first one leads to a strictly linear Guyer–Krumhansl equation while the second one yields a semilinear Guyer–Krumhansl equation, with material functions depending on the temperature. The problem of the local form of first and second law in weakly nonlocal thermodynamics is critically revisited. Different approaches to the extended irreversible thermodynamics, through Jeffrey's type constitutive equations, are analyzed too.

The paper ends with a comparison of different theories and a discussion of future perspectives in non-equilibrium thermodynamics.

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[1] By rational thermodynamics we mean the thermodynamic theory founded in the late 1950s by C. A. Truesdell, W. Noll, R. Toupin, B. D. Coleman et al.

[2] By extended thermodynamics, we mean those thermodynamic theories which include in the state space the dissipative fluxes, such as the heat flux and the stress tensor. In the realm of extended thermodynamics we distinguish between rational extended thermodynamics, proposed by I. Müller and T. Ruggeri [11], and extended irreversible thermodynamics, developed by D. Jou, G. Lebon, and J. Casas-Vázquez [12, 13]. Among the many differences between the two approaches, the most important one with respect to the subject of the present paper is that the first theory assumes that the state space is strictly local while the second one allows a nonlocal state space. When dealing with a common property we avoid this distinction and simply refer to the extended thermodynamics.

[3] By classical irreversible thermodynamics we refer to the theory founded by L. Onsager [16, 17] in the early 1930s and developed by S. R. De Groot, P. Mazur, I. Gyarmati, J. Meixner et al. [15]. In such a theory one can find also an extended approach, with the dissipative fluxes regarded as state variables [18, 19].

2. Cattaneo paradox

2.1. The classical heat equation

The classical Newtonian mechanics does not impose any limit to the speed of thermo-mechanical perturbations. However, in some recent approaches to non-equilibrium thermodynamics, in order to prevent the instantaneous propagation of disturbances, the model equations have been formulated in the hyperbolic form. Notwithstanding, some equations of continuum thermodynamics, such as those of Navier–Stokes and Fourier, are parabolic. This fact has prompted the foundation of a new thermodynamics, developed by several authors in the last two decades, the extended thermodynamics [11, 12].

It is worth noticing that the "paradoxical" theories are able to describe a wide class of physical phenomena. Moreover, as pointed out by Fichera [4] and Day [5,6], in some cases their paradoxical nature is only apparent (see also [20]). In other cases, such as the second sound propagation at low temperature [21–23], these theories are not applicable because the experimental conditions ensuring their validity are not verified.

Let us consider a rigid heat conductor and let us suppose that its thermodynamic state space is spanned by the absolute temperature θ together with its gradient. In the absence of heat sources the local balance of energy reads

$$\dot{e} + q_{i,i} = 0, \tag{1}$$

where $i = 1, 2, 3$, a superposed dot means the partial time derivative, while the subscript $(, k)$ denotes the partial space derivative with respect to the coordinate x_k, e is the density of internal energy, and $\mathbf{q}$ the heat flux vector [24]. By postulating the linear constitutive equations

$$e = c_v\theta, \quad q_i = -k\theta_{,i}, \tag{2}$$

where the volumetric heat capacity c_v and the thermal conductivity k are supposed to be constant, we obtain the classical diffusion equation

$$\dot{\theta} = \frac{k}{c_v}\Delta\theta. \tag{3}$$

2.2. Infinite speeds of propagation

Let us consider now the Cauchy problem for a semi-infinite wire, which we represent by the nonnegative real axis ($x \geq 0$). We suppose that at the initial instant $t = 0$ the temperature, in a given system of units, takes the value 1

for $x = 0$ and vanishes for $x > 0$. Thus we get the following initial value problem:

$$\dot{\theta} = \frac{k}{c_v}\theta_{xx},\tag{4}$$

$$\theta(x \neq 0, 0) = 0, \quad \theta(0, 0) = 1,\tag{5}$$

whose solution for $t > 0$ is[4]

$$\theta(x, t) = \frac{1}{2\sqrt{\dfrac{\pi kt}{c_v}}}e^{-\frac{x^2}{4\frac{k}{c_v}t}}.\tag{6}$$

By Eq. (6) it follows that for $t > 0$ and x^* as large as we wish it, $\theta(x^*, t) > 0$ results i.e., the heat has propagated from $x = 0$ to $x = x^*$ in an interval of time no matter how small. This leads to the conclusion that the speed of propagation of heat is infinite [1]. Such a property was considered by many authors to be paradoxical.

2.3. Paradox removed

In order to remove the paradox, in 1948 Cattaneo [1] proposed his celebrated evolution equation for the heat flux

$$\tau_R\dot{q}_i + q_i = -k\theta_{,i},\tag{7}$$

wherein τ_R is a constant relaxation time. Such an equation inspired several generalizations of the classical heat conduction theory [25, 26, 28].

For the semi-infinite wire considered above, by Eqs. (1) and (7), it follows the telegraphic equation

$$\tau_R\ddot{\theta} + \dot{\theta} = \frac{k}{c_v}\theta_{xx},\tag{8}$$

which allows the propagation of temperature pulses with finite speed,

$$U = \sqrt{\frac{k}{\tau_R c_v}}.\tag{9}$$

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[4]Of course, function θ given by Eq. (6) satisfies Eqs. (4)–(5) only in the sense of the distributions (see [4] for more details).

3. Heat conduction at low temperature

3.1. Phonon gas hydrodynamics

At first, Cattaneo's proposal did not receive much attention inside the mathematical community, which had been faced with parabolic equations for one century. However, it was rediscovered by physicists at the end of the 1960s, when second sound propagation in crystals was detected. Second sound, i.e., thermal wave propagation, is a typical low-temperature phenomenon which can be observed, for instance, in dielectric crystals such as sodium fluoride (NaF) and bismuth (Bi) [21–23]. From the microscopic point of view, the heat transport at low temperature is modelled through the phonon gas hydrodynamics [29, 30]. In a solid crystal at low temperature the phonons form a rarefied gas whose kinetic equation can be derived similarly to that of an ordinary gas. Moving through the crystal lattice they undergo two different types of scattering:

i) Normal (N) scattering, conserving the phonon momentum;
ii) Resistive (R) scattering, in which the phonon momentum is not conserved.

The frequencies ν_N and ν_R of normal and resistive scattering determine the characteristic relaxation times $\tau_N = \dfrac{1}{\nu_N}$ and $\tau_R = \dfrac{1}{\nu_R}$. Diffusive heat transport takes over when ν_R tends to infinity and hence $\tau_R = \dfrac{1}{\nu_R}$ tends to zero. If instead $\tau_N = \dfrac{1}{\nu_N}$ tends to zero, then a wave-like energy transport may occur. In such a case the evolution of the heat flux is well described by Eq. (7). However, the available experimental results show that the material functions k, c_v, and τ_R are no longer constant but depend on the absolute temperature θ.

3.2. Material parameters near the critical temperature

Usually, at low temperature crystals exhibit a maximum of the heat conductivity around a critical point, which depends on the purity of the material.

The functions e and k can be determined from experimental data, e.g., in the case of NaF, cf. [22]. Moreover, there are also data available for the speed of second sound pulses in dependence of the absolute temperature θ [22, 31].

The heat conductivity in NaF [22] is well fitted by the family of functions given by

$$k(\theta) = e^{e^{a + b \ln, \theta + c \ln^2, \theta}}. \tag{10}$$

In the sense of least squares method, one gets the best fit of the data with

$$a = -7.15, \quad b = 6.53, \quad c = -1.20,$$

where k is measured in W/cmK. The measured arrival times of the heat pulses allow the identification of τ_R experimentally.

We denote by U_E the speed of a wave running through a material at an equilibrium state, i.e., with $\mathbf{q} \equiv \mathbf{0}$. In NaF it depends on the temperature according to the linear law

$$U_E = \alpha + \gamma \theta$$

with

$$\alpha = 0.41 \, cm/\mu s, \quad \gamma = -0.01 \, cm/\mu sK.$$

For the dependence of the specific heat on the temperature, Debye's law,

$$e = e_0 \theta^4 / 4, \tag{11}$$

with $e_0 = 2.3 \, J/cm^3 K^4$, has been found to be valid.

From the data above the relaxation time τ_R can be calculated by the relation

$$\tau_R = \frac{k}{U_E^2 c_v}. \tag{12}$$

3.3. Diffusive and hyperbolic heat conduction

Near the critical point second sound appears. The diffusive non-Fourier heat transport takes over in the neighborhood of the critical point where both relaxation times are not negligible. This introduces dissipation and regularizes the profile of the pulses, which, however, can still be observed [32]. Often such a phenomenology is referred to as diffusive-hyperbolic heat conduction. This definition comes from the observation that diffusive effects are superposed to thermal wave propagation. It can be described by the Guyer–Krumhansl equation [7, 8]:

$$\tau_R \dot{q}_i + q_i = -k\theta_{,i} + \frac{9}{5} \frac{k\tau_N}{c_v} \left(q_{i,kk} + 2q_{k,ki} \right). \tag{13}$$

Such an equation, which generalizes Eq. (7), was the first in the literature to include both relaxation times. The material coefficient τ_N also depends on the temperature. According to experimental observations [21], one can get

$$\tau_N \propto \theta^{-m},$$

with $m \in \{3, 4, 5\}$ depending on the material.

At a certain distance from the maximum of the heat conductivity, both the relaxation times become negligible, the pulses disappear, and the Fourier diffusive regime takes over. The different regimes described so far are illustrated in Figures 1–3 below, which, along the direction orthogonal to the plane $\{x, t\}$, show the evolution in space and time of an initial temperature perturbation of $1\,K$.
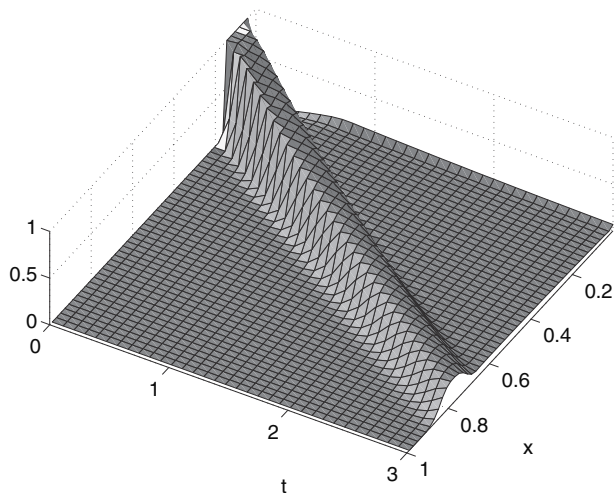
Figure 1   Hyperbolic heat conduction near the critical temperature.
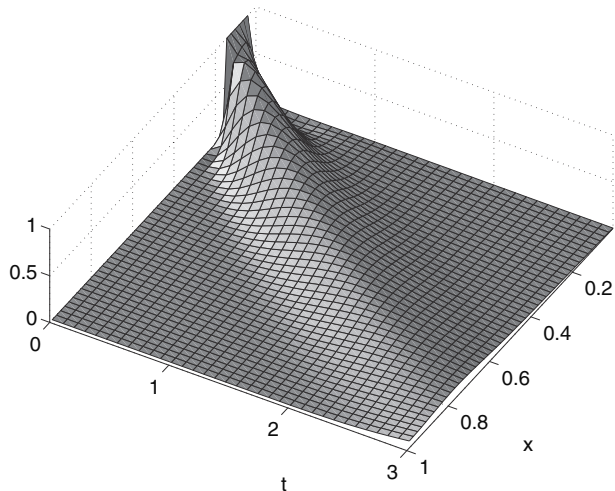
Figure 2   Diffusive-hyperbolic heat conduction.
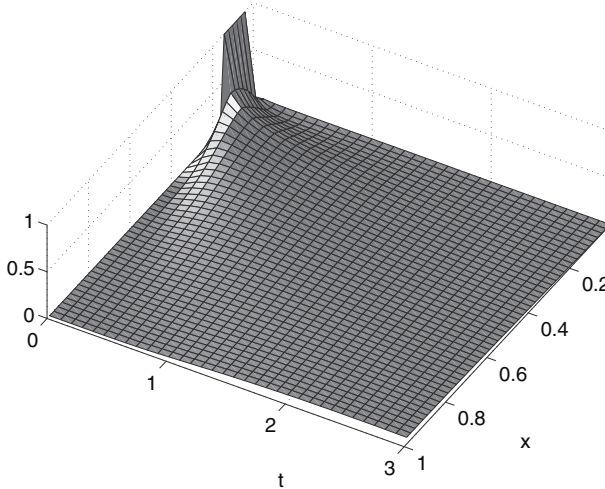
Figure 3   Transition to the Fourier diffusive regime.

4.   Rational thermodynamics of heat conduction

4.1.   Internal state variables

In rational thermodynamics the fundamental balances are that of mass density, linear and angular momentum and energy. Moreover, some additional governing equations, not necessarily in the balance form, can describe the evolution of internal parameters. The dissipative fluxes, such as heat flux and stress tensor, do not enter the state space but are assigned through suitable constitutive equations [9, 10, 33]. In the absence of heat source, for the rigid heat conductor considered here we have only the balance of energy (1). Moreover, the second law of thermodynamics reads

$$\dot{s} + J_{i,i} \geq 0, \tag{14}$$

where s is the entropy density and $\mathbf{J}$ is the entropy flux. A fundamental assumption of rational thermodynamics is represented by the constitutive equation

$$J_i = \frac{q_i}{\theta}. \tag{15}$$

It is worth noticing that in the other thermodynamic theories the previous assumption is questioned and more general expressions for the entropy current are postulated. We will see in Section 7 that also in rational thermodynamics such a hypothesis can be substituted by a weaker one.

Equation (15), together with Eqs. (1) and (14), leads to the celebrated Clausius–Duhem inequality

$$\dot{\psi} + s\dot{\theta} + \frac{q_i}{\theta}\theta_{,i} \leq 0,\tag{16}$$

with the Helmholtz free energy $\psi = e - s\theta$.

There are several attempts to make compatible the requirement of finite speed of propagation with the general principles of rational thermodynamics [25–27]. Internal state variables offer a valid support to achieve that task. These variables allow the description of non-equilibrium processes involving complex thermodynamical systems [34–39]. In particular, they can be used to model heat conduction in solid crystals at low temperature [40–42].

These additional parameters are usually introduced through ordinary differential equations, called kinetic equations, on the basis of the physical experiments.[5] However, this is not the most general case since a large number of physical phenomena are directly amenable by means of spatially nonuniform internal variables [36, 43–49], whose evolution is determined by complete balance laws, including both a rate term and a divergence term. Then, we are faced with a gradient theory.

4.2. Dynamical temperature

In the framework of gradient generalization to the internal state variable approach, a new theory of heat conduction was developed by Kosiński and co-workers [42,45,50–55], which was designed to be consistent with rational thermodynamics and capable of describing heat waves.

An additional scalar state variable β was introduced.

At equilibrium β is a function of the classical absolute temperature θ, otherwise β follows after θ with a certain delay, controlled by a relaxation time τ_R. This delay introduces hyperbolicity and, in the limit of vanishing relaxation time, determines the transition to the classical parabolic case.

Besides the energy balance (1), the kinetic equation

$$\dot{\beta} = f(\theta, \beta),\tag{17}$$

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[5]Sometimes the name internal variables denotes those non-equilibrium parameters which at the equilibrium reduce to a function of the standard ones. The variables which instead vanish at the equilibrium are referred to as dynamic degrees of freedom [14].

with f to be determined through second sound measurements, is postulated. Moreover, the constitutive equations

$$q_i = -k\beta_{,i}, \tag{18}$$

$$\psi = \psi(\theta, (\beta_{,i})^2), \tag{19}$$

are given. These equations allow identifying the function $(\frac{\partial f}{\partial \theta})^{-1}$ with the variable relaxation time τ_R appearing in Eq. (7).

The following thermodynamic restrictions are easily proved:

$$s = -\frac{\partial \psi}{\partial \theta}, \tag{20}$$

$$q_i = -\theta \frac{\partial f}{\partial \theta} \frac{\partial \psi}{\partial \beta_{,i}}. \tag{21}$$

By Eqs. (18), (21), and (10), it follows that τ_R cannot depend on β. Consequently,

$$f(\theta, \beta) = f_1(\theta) + f_2(\beta). \tag{22}$$

Moreover,

$$\psi = \psi_1(\theta) + \frac{1}{2}\psi_2(\theta)(\beta_{,i})^2, \tag{23}$$

where

$$\psi_2(\theta) = \frac{k(\theta)\tau_R(\theta)}{\theta}. \tag{24}$$

Finally, by comparison of Debye's law (11) with

$$e = \psi + \theta s = \psi - \theta \frac{\partial \psi}{\partial \theta}, \tag{25}$$

we infer

$$\psi_1 - \theta \frac{d\psi_1}{d\theta} = e(\theta), \tag{26}$$

$$\psi_2 - \theta \frac{d\psi_2}{d\theta} = 0. \tag{27}$$

Hence, $\psi_2 = \psi_{2_0}\theta$, and consequently, by the definition of ψ_2,

$$k(\theta)\tau_R(\theta) = \psi_{2_0}\theta^2. \tag{28}$$

So, from this equation together with the definition of τ_R we obtain a thermodynamic compatibility condition for the right-hand side of the kinetic equation:

$$\tau_R(\theta) = \left(\frac{\partial f}{\partial \theta}\right)^{-1} = \frac{\psi_{2_0}\theta^2}{k(\theta)}. \tag{29}$$

From this f_1 can be determined up to a constant by integration of the differential equation

$$\psi_{2_0}\frac{df_1}{d\theta} = \theta^{-2}k(\theta). \tag{30}$$

Let us assume $f_2 = -f_1$, in such a way that the integration constant does not enter the model. The above expression of ψ_2 leads to an entropy function, which ensures that the principle of maximum entropy at equilibrium is fulfilled.

4.3. Heat waves

For numerical solutions the data for the considered initial and boundary value problem have been chosen to be in accordance with the heat pulse experiment for NaF reported in [22].

At the left-hand side of a specimen of pure NaF, the temperature is raised from the uniform value θ_0 to the value $\theta_0 + imph$ (impulse height) for a short time *impd* (impulse duration). At the right-hand side, the temperature is measured via the changes of an electrical resistance.

The initial temperature is 15 K, the impulse height 1.0 K, the impulse duration is 0.2 μs, the length of the specimen 8.3 mm.

Typical numerical results are visualized in Figures 4 and 5.

In Figure 4, where the initial temperature is $\theta_0 = 15$ K, a well-determined second sound signal is evident. When the temperature is raised above 20 K, we observe the transition to the Fourier diffusive regime represented in Figure 5.
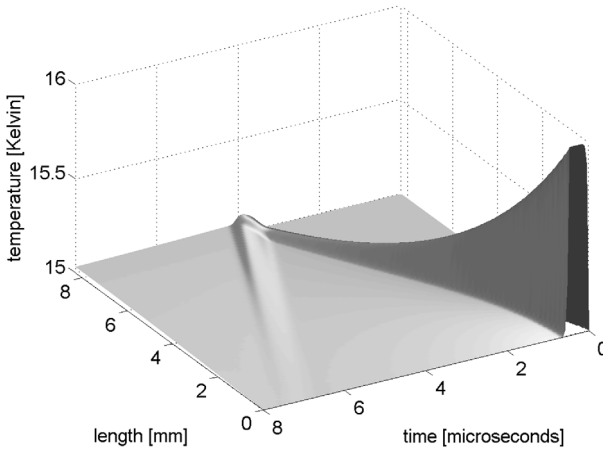
Figure 4 Second sound propagation in NaF. (θ_0, $= 15$ K, $imph = 1$ K, $impd = 0.2\mu$ s, length of the specimen 8.3 mm).
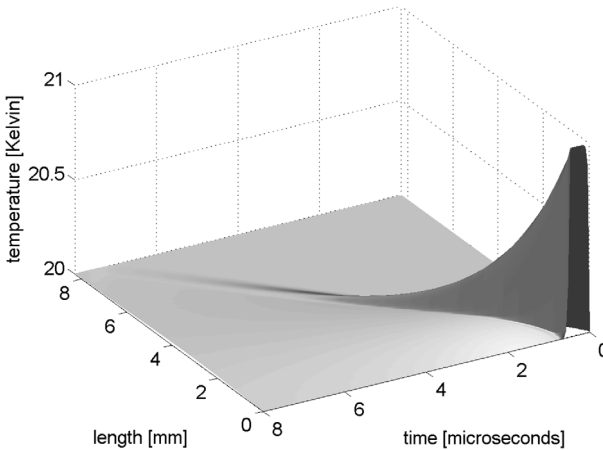
Figure 5 Fourier diffusive regime in NaF. (θ_0, $= 20$ K, $imph = 1$ K, $impd = 0.2\mu$ s, length of the specimen 8.3 mm).

5.   Rational extended thermodynamics of heat conduction

5.1.   Hierarchical system and extended state space

Rational extended thermodynamics [11, 56] is one of the "nonconservative" remedies to the problem of infinite pulse speeds. Actually, it is a hierarchy of theories with an increasing number of fields. The system of governing equations is given by an arbitrary number of balance laws, in which the flux at step n becomes the wanted field at step $n + 1$. The choice of the equation number depends on the characteristic of the phenomenon considered.

The evolution in time of the unknown fields is governed by the following first-order hierarchical system of balance laws:

$$\dot{F} + F_{k,k} = r, \tag{31}$$

$$\dot{F}_k + F_{kj,j} = r_k, \tag{32}$$

$$\dot{F}_{kj} + F_{kji,i} = r_{kj}, \tag{33}$$

$$\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

$$\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

$$\dot{F}_{kji\ldots p} + F_{kji\ldots pq,q} = r_{kji\ldots p}, \tag{34}$$

where functions **r** represent the productions of the unknown fields, while functions **F** denote the fluxes at the step n but also the unknown fields at the step $n + 1$. To close the system (31)–(34), one needs constitutive equations for the last flux in the hierarchy $F_{kji\ldots pq}$, and for the productions $r, r_k, r_{kj}, \ldots$, $r_{kji\ldots p}$, too. The constitutive quantities will depend on all the wanted fields but are independent of their gradients. This mathematical structure stems from statistical mechanics [57], since a fundamental hypothesis of rational extended thermodynamics is to make its results compatible with those of the microscopic theories [11, 12].

5.2.   Extended thermodynamics of phonons

In order to model heat conduction at low temperature, in rational extended thermodynamics the balance equations of phonon gas hydrodynamics are applied [28]. The wanted fields are the internal energy e, the three components p_i of the first moment of the system of governing equations of phonon gas hydrodynamics, connected to the heat flux by the relation $q_i = c^2 p_i$, where c means the Debye phonon velocity [29, 30], and the six independent components of the (symmetric) flux of moment $N_{(ij)}$, $(i, j = 1, 2, 3)$[6]. Here and in the next section we assume that c is constant. Such an assumption is not perfectly in accordance with the experimental evidence [32, 58], however it is suitable for describing the main properties of second sound propagation. The interrelation of the traces of consecutive currents, following the kinetic theory, in the present case is expressed by $N_{(ii)} := e$. Therefore, it is convenient to decompose the flux $N_{(ij)}$ into a spherical and a deviatoric part, according to the equation [28]

$$N_{(ij)} = \frac{1}{3} e \delta_{ij} + N_{<ij>}, \tag{35}$$

---

[6]Here and in the following, the symbol $t_{(ij)}$ will denote symmetric tensors while $t_{<ij>}$ will be used to indicate symmetric traceless tensors.

where $N_{<ij>}$ is symmetric and traceless. Due to the decomposition above, the energy density coincides with the trace of $N_{(ij)}$. As a consequence, we have only nine independent thermodynamic variables, namely e, p_i, and the five independent components of $N_{<ij>}$. These nine variables obey the generic hierarchical balance equation [28]

$$\dot{F}_{(i_1...i_M)} + c^2 \frac{M}{2M+1} F_{(i_1...i_{M-1}),i_M} + F_{(i_1...i_M i_{M+1}),i_{M+1}} = P_{(i_1...i_M)}, \quad (36)$$

where $F_{(i_1...i_M)}$, $F_{(i_1...i_M i_{M+1})}$, and $F_{(i_1...i_{M-1})}$ denote the fluxes of order M, $M+1$, and $M-1$, respectively, while $P_{(i_1...i_M)}$ means the production of order M. Let us take

$$F_0 = \frac{e}{c^2}, \qquad F_{i_1} = p_k, \qquad F_{(i_1 i_2)} = N_{<hk>}. \quad (37)$$

In such a case the constitutive equations for the productions are [28]

$$P_0 = 0, \qquad P_{i_1} = -\frac{1}{\tau_R} p_k, \qquad P_{(i_1 i_2)} = -\frac{1}{\tau} N_{<hk>}, \quad (38)$$

where

$$\frac{1}{\tau} = \frac{1}{\tau_R} + \frac{1}{\tau_N} \quad (39)$$

is the total collision frequency. Then, the balance (36), evaluated for $M = 0, 1, 2$, yields the system

$$\dot{e} + c^2 p_{k,k} = 0, \quad (40)$$

$$\dot{p}_k + \frac{1}{3} e_{,k} + N_{<kh>,h} = -\frac{1}{\tau_R} p_k, \quad (41)$$

$$\dot{N}_{<hk>} + c^2 \frac{2}{5} p_{<h,k>} + F_{<hk>m,m} = -\frac{1}{\tau} N_{<hk>}, \quad (42)$$

where $F_{<hk>m}$ is the flux of $N_{<hk>}$, to be assigned through a constitutive equation. Below we reinspect two particular cases of the system (40)–(42), which are often used in modelling heat wave propagation at low temperature.

5.3. The 4-fields and 9-fields systems

The 4-fields system holds if the effects due to $N_{<hk>}$ can be neglected. It is able to describe qualitatively second sound effects. The governing system is

$$\dot{e} + c^2 p_{k,k} = 0, \quad (43)$$

$$\dot{p}_k + \frac{1}{3}e_{,k} = -\frac{1}{\tau_R}p_k. \tag{44}$$

The calculated values of wave speeds are only qualitatively in accordance with the measured ones [28].

The 9-fields system holds if the effects due to $F_{<hk>m}$ can be neglected. We get so

$$\dot{e} + c^2 p_{k,k} = 0, \tag{45}$$

$$\dot{p}_k + \frac{1}{3}e_{,k} + N_{<kh>,h} = -\frac{1}{\tau_R}p_k, \tag{46}$$

$$\dot{N}_{<hk>} + c^2\frac{2}{5}p_{<h,k>} = -\frac{1}{\tau}N_{<hk>}. \tag{47}$$

Again, the calculated values of wave speeds give only a qualitative agreement with the measured ones [28]. Finally, both the systems above are not able to reproduce the diffusive-hyperbolic regime.

6.   Classical irreversible thermodynamics of heat conduction

6.1.   The wave approach to thermodynamics

In classical irreversible thermodynamics the system of equations governing the evolution of the unknown fields is not required to present any particular structure. The fields can be ruled either by partial differential equations (not necessarily in the balance form) or by ordinary differential equations. Its basic postulate is the local-equilibrium hypothesis, according to which certain thermodynamic functions which are well defined only at the equilibrium states, such as temperature or entropy, are well-suited to describe non-equilibrium states too [14, 15, 18]. Besides the conventional extensive or intensive state variables, such as energy, deformation, and/or internal state variables, the dissipative fluxes are allowed to enter the set of the independent thermodynamic variables [18, 19].

As far as the heat transport is concerned, besides the balance of energy (1) we have an evolution equation for $\mathbf{q}$ whose form can be determined by exploiting the second law [14, 15, 18]. To this end, the entropy inequality must be reduced to a sum of products between undetermined functions and given functions, both defined on the constitutive space. In such a way the undetermined functions can be represented as linear combinations of the given functions [14, 15, 18]. The following constitutive equations are postulated

$$s(e, q_i) = s_E(e) + \frac{1}{2}m_{ij}q_iq_j, \tag{48}$$

$$J_i = \frac{\partial s}{\partial e} q_i, \tag{49}$$

where $s_E(e)$ is the local equilibrium entropy and m_{ij} is a negative defined second-order tensor. The expression (48) above is suggested by the representation theorem for scalar functions depending on vector variables and by the principle of maximum entropy at equilibrium [14]. On the other hand, due to Eqs. (48), (49), and (1), one can get the following form of the entropy inequality (14):

$$\left((\frac{\partial s}{\partial e})_{,i} + \frac{1}{2} \left(\frac{\partial m_{ij}}{\partial q_k} q_j \right) \dot{q}_k + m_{ij} \dot{q}_j \right) q_i \geq 0. \tag{50}$$

The coefficient in front of $\mathbf{q}$ contains only one undetermined quantity, namely $\dot{\mathbf{q}}$. Therefore, the inequality above can be solved as

$$(\frac{\partial s}{\partial e})_{,i} + \frac{1}{2} \left(\frac{\partial m_{ij}}{\partial q_k} q_j \right) \dot{q}_k + m_{ij} \dot{q}_j = L_{ij} q_j, \tag{51}$$

where, in general, the tensor L_{ij} depends on the state variables. Let us observe that, due to the presence of the term $(\frac{\partial s}{\partial e})_{,i}$ the evolution equation above depends also on the gradient of $\mathbf{q}$, i.e., it is a partial differential equation. As a particular case, if m_{ij} is constant, this equation can reduce to the classical Cattaneo equation with variable material functions.

It is worth noticing that sometimes the classical techniques of exploitation of the second law, namely the Liu procedure [59, 60] or the Coleman–Noll procedure [33], are used jointly with the previous one. The method results in the application of the above analysis to the reduced entropy inequality following these procedures [61–65]. However, it seems to be important to note that the technique above is the only one which is capable of giving a set of differential equations as thermodynamic restrictions.

6.2. Evolution of higher order fluxes

Let us consider now the case of two dissipative fluxes entering the constitutive space [64]. The equilibrium variable will be the internal energy e, while the first dynamic variable is supposed to be the heat flux itself. As a further dynamic variable, let us choose a second-order tensor $\mathbf{\Psi}$ whose components will be denoted by Ψ_{ij}, $i, j = 1, 2, 3$.

We postulate the constitutive equation as

$$F = F^*(e, q_i, \Psi_{ij}), \tag{52}$$

where F means an element of the set of constitutive functions $\{s, \mathbf{J}\}$. In fact, as in the previous case, we assign a constitutive equation for the couple $\{s, \mathbf{J}\}$ and apply the procedure illustrated in the previous section to obtain evolution equations for q_i and Ψ_{ij}. The basic thermodynamic state space is spanned by the 13 unknown quantities $\{e, q_i, \Psi_{ij}\}$. Besides the balance of energy, the system of evolution equations for the 12 wanted fields q_i and Ψ_{ij} is needed. In order to derive such a system, let us calculate σ_s according to the classical procedures of irreversible thermodynamics. Along with Gyarmati [18] and Verhás [66], we represent the entropy function, out of local equilibrium, as

$$s(e, q_i, \Psi_{ij}) = s_E(e) + \frac{1}{2} m_{ij} q_i q_j + \frac{1}{2} n_{ijkl} \Psi_{ij} \Psi_{kl}. \tag{53}$$

In Eq. (53) the matrices m_{ij} and n_{ijkl} are constitutive functions depending on the basic fields e, q_i, and Ψ_{ij}. The principle of maximum entropy at the equilibrium forces m_{ij} and n_{ijkl} to be negative definite. Moreover, let us assume that they take the form

$$\mathbf{m} = -m\mathbf{I}, \quad \mathbf{n} = -n\mathbf{I}, \tag{54}$$

where m and n are positive real coefficients and $\mathbf{I}$ means the unitary tensor in the corresponding tensorial space. Finally, along with Verhás [66], let us represent the entropy current as

$$J_i = \frac{\partial s}{\partial e} q_i + \frac{\partial s}{\partial q_j} \Psi_{ji}. \tag{55}$$

One should notice that the previous form of the entropy current is not the most general one and some alternative forms are also possible (see for instance [67, 68]).

Finally, according to arguments from the kinetic theory, we assume that $\mathbf{\Psi}$ is symmetric [11, 12, 28]. Under the simplifications above, exploitation of the second law through the procedure illustrated in Section 6.1, leads to [64]

$$\dot{q}_i + \Psi_{(ik),k} = -\frac{1}{m} \left(R_{(ik)} q_k + S_{(ikl)} \Psi_{(kl)} - \frac{\partial^2 s_0}{\partial e^2} e_{,i} \right), \tag{56}$$

$$\dot{\Psi}_{(ij)} = -\frac{1}{n} \left(U_{(ijk)} q_k + V_{(ij)(kl)} \Psi_{(kl)} \right) - \frac{m}{n} q_{(i,j)}. \tag{57}$$

From Eqs. (56)–(57) it results that the evolution of $\mathbf{q}$ is ruled by a set of balance laws with gradient dependent source terms, while tensor $\mathbf{\Psi}$ obeys a set of ordinary differential equations.

6.3. The 4-fields and 9-fields systems recovered

If one assumes $\Psi_{(ij)} = \frac{1}{3}c^2 e \delta_{ij}$, then the 4-fields system of the previous section is recovered by Eqs. (56) and (57). In fact, if in (56) we assume

$$S_{(ikl)} = 0, \quad R_{(ij)} = \frac{m}{\tau_R}\delta_{ij}, \tag{58}$$

then we get

$$\dot{p}_i + \left(\frac{1}{3} - \frac{1}{mc^2}\frac{\partial^2 s_0}{\partial e^2}\right)e_{,i} = -\frac{1}{\tau_R}p_i. \tag{59}$$

On the other hand, due to the high speed of phonons $\left(42 \times 10^4 cmsec^{-1}\right.$ in NaF [53]$\left.\right)$, the coefficient $\frac{1}{mc^2}\frac{\partial^2 s_0}{\partial e^2}$ in Eq. (59) can be neglected whenever the absolute temperature $\theta = \left(\frac{\partial s}{\partial e}\right)^{-1}$ has no jumps, i.e. whenever the Lax conditions for shock wave formation [55, 56, 69–71] are not fulfilled. In such a case Eq. (59) reduces to Eq. (44). Furthermore, assuming

$$U_{(ij)k} = 0, \quad V_{(ij)(kl)} = 0, \quad \frac{m}{n} = c^2, \tag{60}$$

and taking into account the decomposition $p_{(i,j)} = \frac{1}{3}p_{k,k}\delta_{ij} + p_{<i,j>}$, Eq. (57) can be rewritten as follows:

$$\frac{1}{3}\dot{e}\delta_{ij} + \frac{1}{3}c^2 p_{k,k}\delta_{ij} + c^2 p_{<i,j>} = 0. \tag{61}$$

Finally, the trace of Eq. (61) yields the balance of energy (43).

In order to obtain the 9-fields system, let us proceed with the identification

$$\Psi_{(ij)} = \frac{1}{3}c^2 e \delta_{ij} + c^2 N_{<ij>}, \tag{62}$$

and let us postulate the constitutive equations,

$$S_{(ikl)} = 0, \quad R_{(ij)} = \frac{m}{\tau_R}\delta_{ij}, \quad U_{(ij)k} = 0, \quad \frac{m}{n} = c^2. \tag{63}$$

Moreover, let us assume

$$V_{(ij)(kl)} = -\frac{m}{3\tau}\delta_{ij}\delta_{kl} + \frac{m}{2\tau}(\delta_{ik}\delta_{jl} + \delta_{il}\delta_{jk}). \tag{64}$$

Then by Eqs, (56) and (57) we get

$$\dot{p}_i + \left(\frac{1}{3} - \frac{1}{mc^2}\frac{\partial^2 s_0}{\partial e^2}\right)e_{,i} + N_{<ij>,j} = -\frac{1}{\tau_R}p_i, \tag{65}$$

$$\frac{1}{3}\dot{e}\delta_{ij} + \dot{N}_{<ij>} + \frac{1}{3}c^2 p_{k,k}\delta_{ij} + c^2 p_{<i,j>} = -\frac{1}{\tau}N_{<ij>}. \tag{66}$$

The trace of Eq. (66) yields the balance of the energy (45). As a consequence of Eq. (45), the last equation reduces to

$$\dot{N}_{<ij>} + c^2 p_{<i,j>} = -\frac{1}{\tau}N_{<ij>}. \tag{67}$$

Also in this case in the absence of shocks Eq. (65) reduces to Eq. (41) while Eq. (67) differs from Eq. (47) only for the coefficient in front of $p_{<i,j>}$. Such a discrepancy is not important at that level since the 9-fields system yields only qualitative agreement with second sound experiments.

An analogous procedure can be applied if the constitutive space is nonlocal. In such a case, the Guyer–Krumhansl equation can be recovered [63].

7. Extended irreversible thermodynamics of heat conduction

7.1. Weakly nonlocal extended thermodynamics

In the present section we show that the Guyer–Krumhansl equation can be recovered in the framework of weakly nonlocal thermodynamics. Such a name denotes a class of theories which introduce the spatial derivatives of the basic variables into the constitutive functions [34, 62, 65]. Nonlocal state spaces constitute a valuable tool in continuum thermodynamics, for instance, to account for material microstructure [35, 36, 43], to achieve nonlocal extensions of classical local theories [32, 42, 44, 46, 72], to model fast phenomena in miniaturized systems [73–75]. However, more familiar cases can arise. Let us mention, as an example, Fourier heat conduction theory in rational thermodynamics [33], where the gradient of the absolute temperature enters the state space.

Extended irreversible thermodynamics constitutes a valuable example of weakly nonlocal theory. Analogously to rational extended thermodynamics, it assumes that the unknown fields are the dissipative fluxes, but in contrast to it, the gradients of these fluxes are permitted to enter the state space [12]. Let us consider a rigid heat conductor with thermodynamic state space spanned by the set $\left(e, e_{,k}, q_i, q_{i,k}\right)$. Besides Eq. (1), in the spirit of extended thermodynamics, we suppose that the heat flux is governed by the balance equation

$$\dot{q}_i + \Phi_{ik,k} = r_i, \tag{68}$$

where Φ_{ik} are the components of the flux of $\mathbf{q}$, and r_i are the components of the production of $\mathbf{q}$. The evolution equation we are looking for can be obtained by the Boltzmann equation for phonons in the Debye approximation, if one maintains terms $O(\tau_N)$ only [7, 8]. For states close to equilibrium, Eq. (13) can be rewritten as follows:

$$\tau_R(T)\dot{q}_i + q_i = -k(T)T_{,i} + \frac{9}{5}\frac{k(T)\tau_N(T)}{c_v(T)}\left(q_{i,kk} + 2q_{k,ki}\right),\qquad(69)$$

where

$$T = \left(\frac{\partial s_E}{\partial e}\right)^{-1}\qquad(70)$$

denotes the local equilibrium temperature. Such a temperature, which is the only one measurable in second sound experiments, will be distinguished by the non-equilibrium absolute temperature θ, defined through the thermodynamic relation

$$\frac{\partial s}{\partial e} = \frac{1}{\theta},\qquad(71)$$

(see [76, 77] for more details).

7.2. The linear Guyer–Krumhansl equation

The differential equation (69) is linear with respect to the heat flux and its space and time derivatives, with scalar coefficients depending on the local equilibrium absolute temperature T only. Such an equation is said to be semi-linear [56]. In order to construct an appropriate thermodynamic model, one can start with the general constitutive equations [72]

$$\Phi_{ij} = A\delta_{ij} + Bq_iq_j - C_1q_{i,j} - C_2q_{k,k}\delta_{ij} - C_3q_{j,i},\qquad(72)$$
$$r_i = -a_0q_i - b_0e_{,i} + f_jq_{j,i} + q_{i,j}h_j + g_iq_{k,k},\qquad(73)$$

where all the coefficients appearing in the expressions above depend on the wanted fields but not on their derivatives. The exploitation of the second law is achieved through the Liu procedure [59]. As a result, one observes that the space nonlocality does not influence the entropy but it does contribute to the entropy flux. For isotropic materials, the following constitutive relation ensues:

$$s(e, q^2) = s_E(e) + \frac{1}{2}\phi(e)q^2,\qquad(74)$$

where $\phi(e)$ is an undetermined, negative definite function of e. Then, by taking into account (71) one is led to

$$\theta^{-1}(e, q^2) = \frac{1}{2}\phi' q^2 + T^{-1}(e). \tag{75}$$

Let us observe that by Eq. (75) one can infer that the absolute temperature reduces to the equilibrium temperature either in the absence of heat flux or if $\phi = \text{const}$. The entropy flux is given by

$$J_i = T^{-1}q_i + \frac{\tau_R}{kT^2}(C_1 q_j q_{j,i} + C_2 q_i q_{j,j} + C_3 q_j q_{i,j}), \tag{76}$$

while the evolution of the heat flux is ruled by the governing equation

$$\tau_R \dot{q}_i + q_i = -kT_{,i} + \tau_R \gamma_1 (q_j q_{j,i} - q_{i,j} q_j) + \tau_R (C_1 q_{i,jj} + C_2 q_{j,ji} + C_3 q_{j,ij}), \tag{77}$$

where the coefficient γ_1 has to be determined by the available experimental data. For states close to equilibrium, i.e., if all the material functions are constant, omitting in Eq. (77) the nonlinear contributions and assuming $C_1 = C_2 = C_3$, one recovers the Guyer–Krumhansl equation (69) if

$$C_1 = \frac{9}{5}\frac{k\tau_N}{\tau_R c_v}.$$

The entropy flux corresponding to the linear Guyer–Krumhansl equation is given by

$$J_i = T^{-1}q_i + \frac{9\tau_N}{5c_v T^2}(2q_j q_{(i,j)} + q_i q_{j,j}). \tag{78}$$

It yields the classical entropy flux of rational thermodynamics for vanishing τ_N.

7.3.   The semilinear Guyer–Krumhansl equation

The constitutive equations (72) and (73) are able to reproduce the semilinear equation (69) too [78]. To this end, the second term in Eq. (72), which is nonlinear in **q**, should be neglected. Moreover, the coefficients A, B, and C_i should depend on the internal energy only. Finally, under the additional hypothesis $C_1 = C_3$, the constitutive equation (72) can be rewritten as

$$\Phi_{(ij)} = \phi_1 \delta_{ij} + \phi_2 q_{(i,j)} + \phi_3 q_{k,k}\delta_{ij}, \tag{79}$$

where the material functions ϕ_i, $i = 1, 2, 3$, are supposed to depend on the internal energy only.

It is worth noticing that by applying a new method of exploitation of the second law, which generalizes the classical Liu procedure (see Section 7.4 below for more detail), in [78] is proved that the constitutive equation (79) is also compatible with nonlocal entropy.

Since the specific heat is nonnegative, there is a one-to-one correspondence between the internal energy and the local equilibrium absolute temperature T. So, we are allowed to regard the material functions ϕ_i, $i = 1, 2, 3$, as depending on T. Furthermore, let us assume $\phi_2 = \phi_3$ and let us write $\phi_1(e(T)) = a(T)$, $\phi_2(e(T)) = \phi_3(e(T)) = b(T)$. Then, still taking into account the semilinear approximation, we get

$$\dot{q}_i + \frac{\partial a}{\partial T} T_{,i} + b(T)\Big(q_{i,jj} + 2q_{k,ki}\Big) = r_i, \tag{80}$$

which represents the evolution equation we are looking for. It yields the Guyer–Krumhansl equation (69) if one assumes

$$a(T) = \int \frac{k(T)}{\tau_R(T)} dT, \tag{81}$$

$$r_i = -\frac{q_i}{\tau_R(T)}, \tag{82}$$

$$b(T) = -\frac{9}{5} \frac{k(T)\tau_N(T)}{c_v(T)\tau_R(T)}. \tag{83}$$

7.4. On the local form of the first and second law in weakly nonlocal thermodynamics

In the realm of weakly nonlocal theories, another problem which deserves consideration is the local form of the first and second law. Let us illustrate it by considering rational thermodynamics of deformable bodies in the Eulerian description. The entropy principle, in its classical formulation [9], imposes that the differential inequality

$$\varrho\dot{S} + \varrho S_{,i}v_i + \left(\frac{q_i}{\theta}\right)_{,i} \geq \varrho\frac{\hat{r}}{\theta}, \tag{84}$$

with ϱ as the mass density, S as the specific entropy, θ as the absolute temperature, $\hat{r}$ as the specific radiative heat supply, v_i, $i = 1, 2, 3$, as the components of the velocity, q_i as the components of the heat flux, is satisfied by any solution of the local balances of mass, linear and angular momentum and energy and, eventually, of additional equations governing the evolution of some other

thermodynamical parameters entering the state space. The classical balances of mass, linear and angular momentum and energy read [24]

$$\dot{\varrho} + \varrho_{,i}v_i + \varrho v_{i,j}\delta_{ij} = 0, \tag{85}$$

$$\varrho\dot{v}_i + \varrho v_{i,j}v_j - T_{ij,j} = \varrho b_i, \tag{86}$$

$$\varrho\dot{\varepsilon} + \varrho\varepsilon_{,i}v_i - T_{ij}v_{i,j} + q_{i,i} = \varrho\hat{r}, \tag{87}$$

with $T_{ij} = T_{ji}$, $i, j = 1, 2, 3$ as the components of the Cauchy stress tensor, b_i as the components of the specific body force, ε as the specific internal energy.

Two rigorous techniques can be applied to derive the restrictions placed by the second law of thermodynamics on the constitutive functions, namely the Coleman–Noll procedure [33] and the Liu procedure [59].

If the classical form (87) and (84) of the first and second law holds, both the techniques yield that only the fluxes can depend on the gradients, while the entropy and the absolute temperature may depend only on the basic fields.

Such a conclusion leads to serious discrepancies, because it renders some important classes of nonlocal materials, such as the Korteweg fluids, incompatible with thermodynamics [79]. Two different proposals, allowing us to circumvent that problem, can be found in the literature.

The first proposal is that no constitutive equation should be postulated for the entropy flux $\mathbf{J}$ [80]. This is equivalent to the introduction into the dissipation inequality of an entropy extra-flux $\mathbf{k} = \mathbf{J} - \dfrac{\mathbf{q}}{\theta}$ such that Eq. (84) becomes

$$\varrho\dot{S} + \varrho S_{,i}v_i + \left(\frac{q_i}{\theta}\right)_{,i} + k_{i,i} \geq \varrho\frac{\hat{r}}{\theta}. \tag{88}$$

The second proposal is that the local balance of energy (87) should be modified by postulating the existence of an energy extra-flux $\mathbf{l}$, due either to matter diffusion, [81], or to the interstitial working of long range interactions [79, 82], such that Eq. (87) reads

$$\varrho\dot{\varepsilon} + \varrho\varepsilon_{,i}v_i - T_{ij}v_{i,j} + q_{i,i} + l_{i,i} = \varrho\hat{r}. \tag{89}$$

However, also accepting one of the two proposals above, problems arise in dealing with first-order nonlocal systems. This is due to the fact that the Coleman–Noll and Liu procedures, even in the presence of extra-fluxes, allow the entropy to depend on the gradients of order m of the unknown fields if and only if the constitutive functions depend on the gradients of order $m + 1$ [33, 79]. It is clear that this leads again to a local entropy in the case of first-order nonlocality.

In some recent papers [78, 83], a different point of view was proposed. By applying a generalized method for the exploitation of the second law [78], it is proved that also the entropy and the absolute temperature are nonlocal. The basic idea of the new exploitation method is to take into account as constraints of the entropy inequality not only Eqs. (85)–(87) but also their gradient extensions, up to the order of the gradients entering the constitutive equations. That way, the number of independent constraints is always equal to the number of independent state variables. In the presence of first-order nonlocalities, the mathematical theory developed in [78] has been applied to study heat conduction in miniaturized systems [73], and second-grade Korteweg-type viscous fluids [83]. In both cases the the entropy is nonlocal, whatever the form of Eqs. (84) and (87) is. It is worth observing that, due to thermodynamic relation (71), a nonlocal entropy implies a nonlocal absolute temperature. Such an observation is particularly interesting in the study of heat conduction in nanosystems, since the nonlocal terms in the temperature contribute important nonlinear terms in the heat transport equation [73]. This is true also if the classical expressions (84) and (87) hold, i.e., also in the absence of extra-fluxes.

Indeed, local constitutive equations are well-suited for discrete systems, such as rarefied gases [57]. In the continuum limit, the behavior of the material in a point depends on its interactions with the closest particles too. From the physical point of view, there is no any evident reason why these interactions should influence only the fluxes and not the thermodynamic potentials.

From the considerations above it follows that in weakly nonlocal thermodynamics the local form of the first and second law is still an open problem and that the extra-fluxes are no longer necessary in order to make higher grade material theories compatible with thermodynamics. This fact does not mean that the extra-fluxes do not exist. For instance, in the classical theory of the mixtures the effects of matter diffusion manifest themselves in the appearance of an additional energy flux related to the chemical potential and to the relative mass flux of each constituent [81]. However, their existence and their independency of the heat flux cannot be assumed in general but should be determined on the base of suitable experimental results. Moreover, although some authors consider the two modifications above of the basic laws of thermodynamics as equivalent [81], it is easy to check that they lead to different sets of thermodynamic restrictions. Hence, the equivalence should be understood only in the sense that both provide a valuable tool in order to render higher grade material theories compatible with thermodynamics. New experiments seem to be necessary to decide which of the two options is the more well-suited from the physical point of view.

7.5. Jeffrey-type constitutive equations

An alternative way to model hyperbolic heat conduction is to postulate that also the rates of the unknown fields enter the state space. This type of constitutive equation was first introduced by Jeffrey [84] to study the wave propagation in the Earth's mantle. Recently, these equations have been used to construct an alternative approach to extended irreversible thermodynamics [85, 86]. Hyperbolic heat conduction through Jeffrey-type constitutive equations was first modelled by Muschik [87], who started from the following balances of energy and entropy for rigid bodies at rest:

$$\dot{e} + q_{i,i} = r, \tag{90}$$

$$\dot{s} + \left(\frac{q_i}{\theta}\right)_{,i} + k_{i,i} \geq \frac{r}{\theta}. \tag{91}$$

Here r is the heat supply for unit of volume while the functions k_i denote the components of the entropy extra-flux. The constitutive equations take the form

$$F = F^*(\nu, \nu^\bullet, \nabla\nu, \nabla\nu^\bullet), \tag{92}$$

where $\nu = \frac{1}{\theta}$ and F is an element of the set $\{e, s, q_i, k_i\}$. Moreover, the symbol $f^\bullet$ denotes the co-rotational time derivative of function f (see [88] p. 6, for details), which is necessary to make Eq. (92) frame-invariant [38, 89, 90]. The compatibility of Eq. (92) with the second law is investigated through the Liu procedure [59], while the reduced entropy inequality is solved by applying the method illustrated in Section 6.1. As a result, one obtains

$$\frac{\partial s}{\partial \nu} - \lambda \frac{\partial e}{\partial \nu} = \hat{a}\nu^\bullet + \hat{b}_i \nu_{,i}, \tag{93}$$

$$q_i + \frac{\partial k_i}{\partial \nu} + (\nu - \lambda)\left(\frac{\partial q_i}{\partial \nu}\right) = \hat{c}_i \nu^\bullet + \hat{d}_{ij} \nu_{,j}, \tag{94}$$

$$\nu - \lambda = \hat{f}\nu^\bullet + \hat{g}_i \nu_{,i}. \tag{95}$$

In the restrictions above, λ denotes the Lagrange multiplier related to the energy balance (90) [59], while the functions $\hat{a}, \hat{f}, \hat{\mathbf{c}}, \hat{\mathbf{b}}, \hat{\mathbf{d}}$, and $\hat{\mathbf{g}}$ depend on the state space. The linearized balance of energy around an equilibrium state yields

$$\frac{\partial e}{\partial \nu}\Big|_{eq} \nu^\bullet + \frac{\partial e}{\partial \nu_{,i}^\bullet}\Big|_{eq} \nu_{,i}^{\bullet\bullet} + \frac{\partial e}{\partial \nu_{,i}}\Big|_{eq} \nu_{,i}^\bullet =$$
$$- \left[-\frac{\partial k_i}{\partial \nu} + \left(\hat{c}_i + \hat{f}\frac{\partial q_i}{\partial \nu}\right)\nu^\bullet + \left(\hat{d}_{ij} + \hat{g}_i \frac{\partial q_j}{\partial \nu}\right)\nu_{,j}\right]_{,i}. \tag{96}$$

It is proved in [87] that the equation above is hyperbolic, thus leading to finite speed of propagation of thermal disturbances.

8.   Conclusions and perspectives

We have examined the different approaches to non-equilibrium thermodynamics starting from a different point of view on the problem of heat conduction with finite wave speeds. We have pointed out that, in spite of the apparent differences, the theories present several similarities. In particular, it seems to be remarkable that some mathematical system of equations that is peculiar to the extended theories can be recovered in the framework of classical irreversible thermodynamics. For some aspects, such a theory is the less general one among those examined here, since it rests on the local-equilibrium hypothesis and on the linearity.[7] However, for the choice of the state space and for the structure of the system of governing equations, it is the most general one. In fact, besides the conventional and the internal variables, also the dissipative fluxes can enter the constitutive equations [18, 19]. Furthermore, no particular structure is required for the system of governing equations, as it happens, for instance, in extended thermodynamics. Unfortunately, some of its methodologies are rather heuristic and not based on rigorous mathematical proof (see [9], Lecture 7, for an extensive discussion). We feel that the problem of providing to such a theory a more robust mathematical structure deserves consideration.

All the quoted theories are able to reproduce some of the main properties of heat conduction at low temperature, but none of them leads to an exhaustive description which is free of technical problems. For instance, the results of Section 7 prove that the Guyer–Krumhansl equation can be recovered in the framework of extended irreversible thermodynamics [12] but it cannot be obtained in rational extended thermodynamics [11] because its derivation requires that the gradients of the wanted fields enter the constitutive equations. On the other hand, the presence of the spatial gradients in the constitutive equation for the flux of heat flux makes the theory parabolic and finite speeds of propagation, in a strict mathematical sense, cannot be expected. This last remark justifies the importance of the Guyer–Krumhansl equation in recent discussions on the physical bases of the extended theories of thermodynamics. In fact, all these theories stem from the requirements of accordance with kinetic theory and finite speed of propagation of the initial perturbations. At first sight, the Guyer–Krumhansl equation, which is a consequence of the kinetic theory, seems to prove that none of them is capable of satisfying both

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[7] It is worth observing that also in the other thermodynamic theories the problem of the existence of the entropy beyond the equilibrium has not yet been solved but only circumvented by postulating that entropy is a primitive concept, which does not require any definition [10].

the requirements above. Indeed, this is not strictly true. In fact, in extended irreversible thermodynamics finite speeds of propagation can be obtained in the generalized sense clarified by G. Fichera [4] and W. A. Day [5, 6]. These authors observed that a correct estimation of the speed of propagation of the disturbances requires that the order of magnitude of the solution of the system of balance equations is compared with that of the error affecting the available experimental data which the theory aims to reproduce. In particular, if after a finite interval of time from the beginning of a physical process the solution of the corresponding system of balance laws is greater than the experimental error only in a compact domain, then we can say that such a solution is experimentally zero outside this domain. As a consequence, it has propagated with finite speed because not all the points of the space have been reached in a finite time. A constitutive principle of weak causality, which is in accordance with this point of view, has been formulated in [20].

On the other hand, in rational extended thermodynamics, one can obtain the Guyer–Krumhansl equation through a suitable approximation of the governing system. To this end one should: (**i**) go further with the hierarchy and consider the balance equation for the flux of heat flux; (**ii**) write this equation in such a way that the relaxation time appears explicitly in front of the time derivative; (**iii**) consider regular solutions and a negligibly small relaxation time; (**iv**) use the obtained equation (now in the divergence form), in order to express the heat flux as a function of its first gradient; (**v**) substitute the new form of the heat flux into the constitutive equation for the flux of heat flux. That way, second derivatives could appear into the balance equation for the heat flux and Guyer–Krumhansl equation could be obtained under suitable approximations. It is worth noticing that such a procedure places the theory very close to the traditional rational thermodynamics since a gradient type constitutive equation together with the parabolic regularization of the solution are recovered through the additional assumption that one of the relaxation times is negligible.

All the aforementioned theories present advantages and disadvantages, depending on the phenomenology to which they are applied.

In rational thermodynamics, memory effects, as those arising in heat conduction with finite speed, can be modelled by integral constitutive equations [91–94], by dynamical constitutive equations [95–99], and by internal state variables [40–42]. In the first approach the balance equations are difficult to solve and sometimes the well-posedness of the relevant Cauchy problem is not guaranteed [100]. In the second approach, the dynamical terms entering the constitutive equation of the heat flux in general do not cope with the requirement of material frame indifference. Hence a special definition of time

derivative, which renders the system of equations much more difficult, must be introduced [38, 87]. On the other hand, the internal variables, which lead to more simple systems of equations, are "not controllable", i.e., their value on the boundary cannot be conditioned through the direct action of external forces [34]. Hence it is difficult to assign appropriate boundary conditions. A fully thermodynamic approach to the problem of boundary conditions in the presence of internal variables has been proposed in [101, 102].

In rational extended thermodynamics, in which the memory effects are instead modelled by the hierarchical system of equations following kinetic theory, the main problems are due to the rapidly increasing number of unknown quantities. The most difficult one is the determination of the appropriate number of equations, i.e., of the step at which the hierarchical system should be truncated [103]. Moreover, also in such a theory the determination of suitable boundary conditions is difficult, since the physical meaning of the higher order fluxes is not clear [104]. The same is true in extended irreversible thermodynamics, where the higher order fluxes are necessary in modelling high-frequency processes [74, 75, 105–109].

At this point it seems natural to investigate wether there exists a more general approach to non-equilibrium thermodynamics which encompasses all the previous ones. This important problem still remains to be solved. To this end, it seems to be unavoidable to modify a little bit the basic postulates of all the theories. Moreover, the requirements of finite speeds of propagation and accordance with the kinetic theory should be revisited. We already observed that finite speeds can be obtained in a generalized sense. On the other hand, if we take a look at the postulates of microscopic theories, we discover that their representation of the physical reality is neither more realistic nor more rigorous than that of the macroscopic theories, since also in this case several approximations are necessary in order to obtain reasonable systems of equations. Hence, in building up a macroscopic model, the direct observation of the phenomenology could give a deeper insight into the mathematical structure of the theory with respect to the molecular approach.

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Exergy Transfer Analysis of Forced Convection in External Flow over a Flat Plate

Shuang-Ying Wu[1],[★], You-Li Zhang[2], and You-Rong Li[1]
[1] College of Power Engineering, Chongqing University, Chongqing, 400044, China
[2] Chongqing Electric Power College, Chongqing, 400053, China

[★]Corresponding author (shuangyingwu@yahoo.com.cn)

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Abstract

On the basis of linear non-equilibrium thermodynamic theory, exergy transfer analyses of laminar and turbulent forced convection are conducted in terms of external flows over a flat plate. Two kinds of non-dimensional concepts involving the definition of the local and mean exergy transfer Nusselt number and non-dimensional exergy flux are incorporated into exergy transfer analysis. The new analytical expressions for the local and mean exergy transfer Nusselt number and non-dimensional exergy flux are adopted to describe the exergy transfer characteristics over a flat plate. By taking air as working fluid, the influences of flat plate geometry, Reynolds number, and other operating parameters on the exergy transfer Nusselt number and non-dimensional exergy flux are examined. It is shown how the flow geometric parameters and Reynolds number, etc., may be selected in order to maximize the exergy utilization associated with a specific external convection process. In addition, the results obtained from exergy transfer analysis are compared with those obtained from traditional heat transfer analysis.

1.   Introduction

External flows with heat transfer occur in many engineering installations. Fluid flow and heat transfer through external flow over a flat plate is one of the fundamental research topics in engineering. Heat transfer processes are generally accompanied by thermodynamic irreversibility or entropy generation. Efficient utilization of energy has become one of the primary objectives in the design of fluid flow and heat transfer processes. The second law analy-

sis is the gateway for optimization in thermal equipments and systems, which makes good engineering sense to focus on the irreversibilities of fluid flow and heat transfer processes. Entropy generation or exergy destruction due to heat transfer and fluid flow through a duct has been investigated by many researchers. Bejan [1–5] was perhaps the first to examine entropy generation in convective heat transfer and reviewed the pedagogical merits of the method and the chronological development of the field. The competition between flow and heat transfer irreversibilities also rules the thermodynamic design of external convective heat transfer arrangements, in which the flow engulfs the solid body (walls) that it exchanges heat with. Bejan [6] analyzed entropy generation in fundamental convective heat transfer of four flow configurations: pipe flow, boundary layer over a flat plate, single cylinder in cross-flow, and flow in the entrance region of a flat rectangular duct, and showed how the flow geometric parameters may be selected in order to minimize the irreversibility. Several other studies followed along these lines, such as for external flows: across cylinders with mixed forced and natural convection [7, 8]. Poulikakos and Johnson [9] obtained a general expression of entropy generation for combined convective heat and mass transfer in external flows and applied the general expression to two fundamental problems of forced convection heat and mass transfer, namely, laminar and turbulent boundary layer forced convection from a flat plate and from a cylinder in crossflow. The second law analysis of combined heat and mass transfer in internal and external flows was carried out by Carrington and Sun [10]. A control volume method was used to establish the rate of entropy generation due to heat and mass transfer, accompanied by fluid friction. Budair [11] has conducted a study to determine the entropy generation of unsteady flow on a flat plate and found that entropy generation in the space between the plates is more considerable at initial times of motion than at later times. Chandrasekar and Baskaran [12] applied a genuine variational principle developed by Gyarmati in the field of thermodynamics of irreversible processes unifying the theoretical requirements of technical, environmental, and biological sciences to study the effects of uniform suction and injection in the heat transfer and boundary layer flow with power function main stream velocity and surface temperature variations, over a wedge.

Recently, the use of exergy analysis in thermal design has been discussed and demonstrated by numerous authors. Exergy is a thermodynamic quantity that represents the available energy. An exergy-based performance analysis is the performance analysis of a system based on the second law of thermodynamics that overcomes the limit of an energy-based analysis. Lior et al. [13] gave a brief review of the method for analyzing the space- and time-dependent exergy and irreversibility fields in processes. Although the objectives of exergy or entropy analysis appear to be obvious, it is very noteworthy to recall that one of

the most important and useful objectives is to evaluate how they change with any changes in the process parameters and configuration. Most of the exergy analyses are nowadays conducted on the system level development, by evaluating the exergy values and changes of component input and output streams and energy interactions. While this can indeed identify the exergy destruction in a system component, it does not deliver detailed information about the specific process phenomena, often space and time dependent, which causes the exergy changes in it. A useful or powerful exergy method should be capable of providing insights on how exergy is utilized or lost in the process and hence of suggesting directions for process improvement and optimization [14].

On the other hand, the convective heat transfer process usually contains momentum transfer and heat transfer, the common essence of which is energy transfer and conversion. In fact, energy transfer and conversion are inevitably accompanied by exergy transfer and conversion. However, energy is conservative in its transfer and conversion processes, while exergy is known to be non-conservative due to the irreversibility of its transfer process. As a result, exergy transfer must have rules of its own, which are different from those of energy transfer. In any process, the use of energy is essentially the use of exergy. But with the further researching of energy transfer, it is found that the energy transferred will be different by its property or energy grade, whose effectiveness will vary with the process, and the whole energy can be divided into an exergy part and an anergy part. Many researchers found that knowing about the mechanism of this kind of energy transfer will be very important and significant for optimal system design, economical control, and high-efficiency energy-saving applications [15]. Since Soma [16] and Dunbar et al. [17] put forward the concept of exergy transfer and its equation, the research on exergy transfer has gained some researchers' attention. Detailed exergy balance equations, exergy transfer rates, and exergy destruction rates for flows in complex configurations have been investigated by Sun and Carrington [18, 19]. These integral equations are applicable where it is not feasible to establish the local velocity, pressure, temperature, and concentration distributions. In Ref. [20], a phenomenological equation of exergy transfer, which indicated the relation between exergy flux, exergy resistance, and exergy-driving forces, was derived by applying non-equilibrium thermodynamics to the second law analysis, and the expressions of the exergy transfer coefficients were simultaneously obtained. A simplified expression for the exergy transfer coefficient by neglecting some minor engineering couplings in exergy transfer processes has been proposed. To date, one of the objectives in studying exergy transfer and conversion for laminar or turbulent flow heat transfer has been to calculate entropy generation or exergy destruction [21]. Wu et al. [22, 23] have studied the exergy transfer characteristics of convective heat transfer through a duct with constant wall heat flux and wall temperature by introducing an exergy

transfer coefficient and defining the local and mean exergy transfer Nusselt number.

As mentioned above, exergy is generally not conserved as energy but destroyed in the system. Exergy destruction is a measure of irreversibility which is the source of performance loss. However, it is pointed out that, whatever the condition is, the entropy generation or exergy destruction is greater than zero in convective heat transfer from the viewpoint of thermodynamics, but from the viewpoint of exergy transfer (profit), the exergy change from convective heat transfer of working fluids may be less than zero under a certain condition, which means the reduction of work ability for working fluids. But this is not the goal of convective heat transfer processes in engineering. Furthermore, heat transfer processes are always applied to transfer exergy for the purpose of availability (exergy) utilization; one always focuses on the amount of gained exergy for a certain fluid in engineering, such as in the field of thermal utilization of solar energy etc. [24] Thus, theoretically and practically, it is important to study the rules of exergy transfer and find out the change range in the process parameters and configuration, where the exergy change from convective heat transfer of working fluids is greater than zero.

Although the entropy or exergy analysis for convective heat transfer through an external flow of a flat plate has been dealt with for quite some time, it has not been systematically approached from the perspective of exergy transfer (not exergy destruction) in a way that is compatible and coherent with engineering applications. It is known that external flow has some flow and heat transfer characteristics which are different from those of internal flow, such as pipe flow. As an extension of the authors' previous works, the objective of this paper is to examine the exergy transfer characteristics of forced convective heat transfer through an external flow over a flat plate with constant wall temperature for laminar and turbulent flow by introducing exergy transfer Nusselt number and non-dimensional exergy flux, which is different from that in the previous literature.

2. Exergy transfer model of convection through external flow

Consider an arbitrary differential element surface of body, whose surface area is $\mathrm{d}A$, suspended in a uniform stream with velocity, u_∞, mass flow rate, G_∞, and temperature, T_∞, as shown as Figure 1. The heat transfer, $\mathrm{d}\Phi$, is driven by the temperature difference between the wall of body, T_w, and free stream, T_∞. In addition, a net drag force, $\mathrm{d}F_\mathrm{D}$, which is transmitted through the body to fluid, is caused by the external flow arrangement. A fixed control volume which surrounds the body is chosen. A fluid flows around the body. The boundaries of the control volume are positioned far away from the body (i.e.,
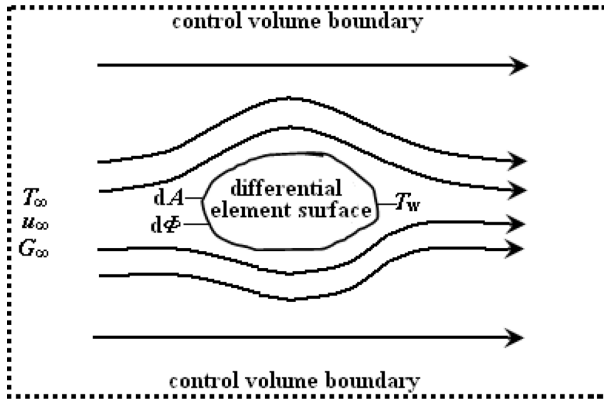
Figure 1   Sketch of control volume over a differential element surface of body through external flow.
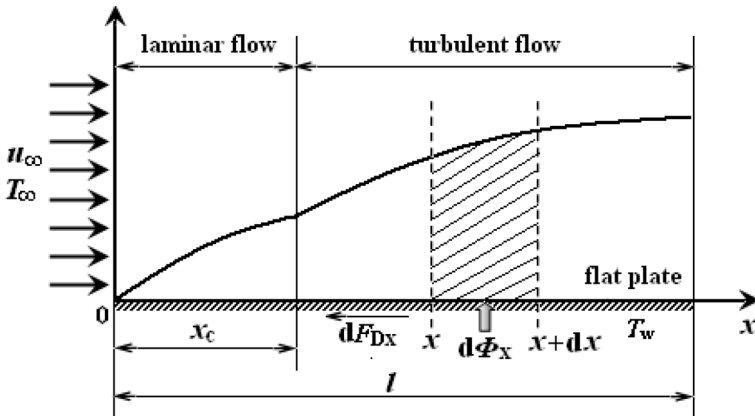

Figure 2   Sketch of forced convective heat transfer process over a flat plate.

the control volume is much larger than the body) such that the conditions at the control volume boundary are unaffected by the body. The control volume can be regarded as a large tube [2].

Using the definition of specific flow exergy,

$$e = h - h_0 - T_0(s - s_0). \tag{1}$$

Considering that $e = f(T, p)$ with $T_0 = \text{const}$, then $\mathrm{d}e$ can be expressed as

$$\mathrm{d}e = \left(\frac{\partial e}{\partial T} \right)_p \mathrm{d}T + \left(\frac{\partial e}{\partial p} \right)_T \mathrm{d}p. \tag{2}$$

According to thermodynamics and the partial derivatives of Eq. (1) with reference to p and T, respectively, the following thermodynamic relations are obtained:

$$\left(\frac{\partial e}{\partial T}\right)_p = c_p \left(1 - \frac{T_0}{T}\right), \tag{3}$$

$$\left(\frac{\partial e}{\partial p}\right)_T = \left(\frac{\partial h}{\partial p}\right)_T - T_0 \left[\frac{1}{T}\left(\frac{\partial h}{\partial p}\right)_T - \frac{1}{\rho T}\right]. \tag{4}$$

Here air is selected as a working fluid, if air is considered as an ideal gas, a state equation and Maxwell's relation may be applied, we have $(\partial h/\partial p)_T = 0$ and $(\partial s/\partial p)_T = -1/(\rho T)$. Thus, Eq. (4) reduces to

$$\left(\frac{\partial e}{\partial p}\right)_T = \frac{T_0}{\rho T}. \tag{5}$$

It should be pointed out that, as the same as an ideal gas, both $(\partial h/\partial p)_T$ and $(\partial s/\partial p)_T$ for an incompressible liquid having constant thermophysical properties, such as water, are also very small. However, when one of them is zero, another must not be zero in order to calculate the entropy generation/exergy destruction caused by pressure drop.

Substituting Eqs. (3) and (5) into Eq. (2), Eq. (2) may be expressed as

$$de = c_p \left(1 - \frac{T_0}{T}\right) dT + \frac{T_0}{T} \cdot \frac{dp}{\rho}. \tag{6}$$

Therefore, the exergy change rate of working fluids over the control volume is given by

$$dE = G_\infty \left[c_p \left(1 - \frac{T_0}{T}\right) dT + \frac{T_0}{T} \cdot \frac{dp}{\rho}\right]. \tag{7}$$

It is assumed that the mean quantities of the control volume are approximately equal to the free stream quantities. This assumption is reasonable since the control volume is much larger than the body, and the same assumption has been used successfully by previous investigators [2, 9]. Thus, Eq. (7) may be rewritten as

$$dE = d\Phi \left(1 - \frac{T_0}{T_\infty}\right) + \frac{T_0 V_\infty}{T_\infty} dp. \tag{8}$$

Considering that the pressure drop of the control volume is caused by the net drag force, dF_D, thus

$$-V_\infty dp = u_\infty dF_D. \tag{9}$$

Combining Eqs. (8) and (9) yields

$$dE = d\Phi \left(1 - \frac{T_0}{T_\infty}\right) - \frac{T_0 u_\infty}{T_\infty} dF_D. \tag{10}$$

Equation (10) is a general expression regarding the exergy change rate of working fluid over an arbitrary differential surface of convection through external flow. It is observed from Eq. (10) that the exergy change rate of working fluid is the result of combined effects caused by finite temperature difference heat transfer and flow pressure drop, namely, the exergy change rate of working fluid is equal to the difference between heat exergy rate derived by the fluid (not heat exergy rate transferred across the boundary surface) and the flow pressure exergy loss rate.

3. Exergy transfer analysis of forced convective heat transfer over a flat plate

As shown in Figure 2, an external flow over a flat plate, which occurs in numerous engineering applications, is considered. It is assumed that the flat plate is sufficiently large. The local exergy change rate of working fluid over a differential element surface of a flat plate may be written as follows according to Eq. (10):

$$dE_x = d\Phi_x \left(1 - \frac{T_0}{T_\infty}\right) - \frac{T_0 u_\infty}{T_\infty} dF_{Dx}. \tag{11}$$

The drag force dF_{Dx} at the wall of the flat plate may be expressed in terms of a friction coefficient C_{fx}:

$$dF_{Dx} = \frac{1}{2} C_{fx} \rho u_\infty^2 dA. \tag{12}$$

The heat transfer rate of the differential element control volume $d\Phi_x$ is

$$d\Phi_x = \alpha_x (T_w - T_\infty) dA. \tag{13}$$

Substituting Eqs. (12) and (13) into Eq. (11), the local exergy change rate of working fluid over a differential element surface of the flat plate becomes

$$dE_x = \alpha_x (T_w - T_\infty) dA \left(1 - \frac{T_0}{T_\infty}\right) - \frac{T_0}{2T_\infty} C_{fx} \rho u_\infty^3 dA. \tag{14}$$

In flow and heat transfer fields, the non-equilibrium conditions are due to the exchange of momentum and energy within the fluid and at the solid boundaries. This non-equilibrium phenomenon causes a continuous generation of

entropy in the flow and heat transfer fields. Every irreversible process can be viewed as the relevant flux driven by the corresponding potential [25–27]. The flux of heat is driven by the temperature gradient, the flux of momentum is driven by the velocity gradient, and the flux of exergy is driven by the temperature gradient and the velocity gradient. Linear non-equilibrium thermodynamics deals with the irreversible transport and rate processes and evaluates the entropy generation/exergy destruction resulting from the irreversibilities taking place in processes by coupling the second law analysis [28]. The linear non-equilibrium thermodynamic description of heat and mass transfer is compatible with the classical engineering approach based on the hydrodynamic theory of boundary layer, with transport coefficients and driving forces [29]. In the linear non-equilibrium thermodynamic analysis, the transport and rate processes are expressed in the form of the phenomenological equations. These equations are capable of displaying the interactions between the various transport and rate processes through the cross phenomenological coefficients [30]. The flows are related to the forces in a linear form with the phenomenological coefficients through phenomenological equations. If the forces vanish, the system goes to an equilibrium state in which the flows are zero. However, it should be pointed out that linear non-equilibrium thermodynamics is based on the local thermodynamic equilibrium assumption, which is the extension of thermodynamic relations in equilibrium systems to local non-equilibrium subsystems. As we know, if a system is not in thermodynamic equilibrium, it means that at least some of the intensive parameters are functions of time and/or position in this system. A local state of a substance is considered as small elementary volumes of the system, and these small volumes should contain a sufficient number of molecules for a macroscopic theory to be applicable. When the local thermodynamic equilibrium holds, thermodynamic parameters in each volume element are evaluated as in a system at equilibrium, and some thermodynamic relations are applicable [31]. The assumption of local thermodynamic equilibrium holds for a great variety of rate processes in physics, chemistry, and biological systems [32].

According to the non-equilibrium thermodynamic theory, potential field gradients can produce irreversible changes, and are called "forces", and denoted by X_k ($k = 1, 2, \ldots, n$) for n gradients. The forces produce certain irreversible phenomena called the "flows" (fluxes) which are symbolized by J_j ($j = 1, 2, \ldots, n$). Generally, any force can cause any flow $J_j (X_k)$ ($j, k = 1, 2, \ldots, n$). Based on the linear relationships between the flow and force, any flow is the result of all the forces and the phenomenological equation is [31]

$$J_j = \sum L_{jk} X_k \quad (j, k = 1, 2, \ldots, n), \tag{15}$$

where L_{jk} is the phenomenological coefficient, represents flow per unit force, and has the characteristics of conductance.

When the exergy flux is influenced by many potential fields, Eq. (15) can be rewritten as

$$q_e = \sum L_{ek} X_{ek} \quad (k = 1, 2, \ldots, n), \tag{16}$$

where L_{ek} is the phenomenological coefficient of exergy flow caused by the kth thermodynamic force X_{ek}. If taking the jth potential field gradient as the driving force of the exergy flux, and the effects of other potential field distributions on the phenomenological coefficient of the exergy flow are still considered, namely, it is assumed that all potential fields' driving forces exert the phenomenological coefficient of the exergy flux in order to compensate the effect of other potential fields on the exergy flux. Thus, Eq. (16) can be expressed as

$$q_e = -\alpha_e(\mu_1, \mu_2, \ldots, \mu_n)\nabla\mu_j. \tag{17}$$

Equation (17) is the field synergy phenomenological law available for engineering exergy transfer processes. Considering that temperature field is coupled with velocity field in convective heat transfer processes, and assuming that the temperature field is the dominant potential field and substituting the potential field gradient with the potential difference, the exergy transfer phenomenological equation of convective heat transfer for the element control volume may be written as follows:

$$d\Phi_{ex} = \alpha_{ex}(T, p)(T_w - T_\infty)dA. \tag{18}$$

The role of the above phenomenological equation is the determination of the transport coefficient. Even though the exergy is not conserved because of irreversibilities caused by the temperature difference heat transfer and flow pressure drop, the aim of exergy change of working fluids is consistent with that of exergy transfer. So the assumption that the exergy change rate of working fluids is equal to the exergy transfer rate of convective heat transfer process is reasonable. Thus, from Eqs. (14) and (18), the local exergy transfer coefficient α_{ex} for forced convection over a flat plate is

$$\alpha_{ex} = \alpha_x\left(1 - \frac{T_0}{T_\infty}\right) - \frac{C_{fx}\rho T_0 u_\infty^3}{2T_\infty(T_w - T_\infty)}. \tag{19}$$

It should be pointed out that the definition of convective exergy transfer coefficient in Eq. (18) serves the exergy change rate of working fluid (not heat exergy rate transferred across the boundary surface) as a reference. However, when the convective heat transfer coefficient is defined, the reference need not be considered, because energy is conservative in its transfer process, and the heat change rate of working fluid is equal to the heat rate transferred across the boundary surface.

3.1.   The local exergy transfer Nusselt number and exergy flux

For an external flow over a flat plate, laminar boundary layer development begins at the leading edge ($x = 0$) and transition to turbulence may occur at a downstream location (x_c) for which a critical Reynolds number Re_c is achieved. The local convective heat transfer coefficient α_x and friction coefficient $C_{f,x}$ of laminar flow and turbulent flow over a flat plate are given by [33].

For laminar flow,

$$\alpha_{x,lam} = 0.332\lambda(u_\infty/v)^{1/2}Pr^{1/3}x^{-1/2} \quad \text{or}$$
$$Nu_{x,lam} = \alpha_x x/\lambda = 0.332Re_x^{1/2}Pr^{1/3}, \quad (20)$$

$$C_{fx,lam} = 0.664Re_x^{-1/2}. \quad (21)$$

For turbulent flow,

$$\alpha_{x,turb} = 0.0296\lambda(u_\infty/v)^{4/5}Pr^{1/3}x^{-1/5} \quad \text{or}$$
$$Nu_{x,turb} = 0.0296Re_x^{4/5}Pr^{1/3}, \quad (22)$$

$$C_{fx,turb} = 0.0592Re_x^{-1/5} \quad (5 \times 10^5 < Re_x < 10^7). \quad (23)$$

Combining Eqs. (20) and (21), (22) and (23) with Eq. (19) and introducing $Re_x = (u_\infty x)/v$, respectively, the local exergy transfer coefficient of laminar flow and turbulent flow over a flat plate are obtained:

$$\alpha_{ex,lam} = 0.332\lambda x^{-1/2}u_\infty^{1/2}v^{-1/2}Pr^{1/3}(1 - T_0/T_\infty)$$
$$-[0.332\rho T_0 v^{1/2}u_\infty^{5/2}x^{-1/2}]/[T_\infty(T_w - T_\infty)], \quad (24)$$

$$\alpha_{ex,turb} = 0.0296\lambda x^{-1/5}u_\infty^{4/5}v^{-4/5}Pr^{1/3}(1 - T_0/T_\infty)$$
$$-[0.0296\rho T_0 v^{1/5}u_\infty^{14/5}x^{-1/5}]/[T_\infty(T_w - T_\infty)]. \quad (25)$$

Equations (24) and (25) express the dependence of the local exergy transfer coefficient on fluid friction and heat transfer for laminar and turbulent flow over a flat plate. The local exergy transfer coefficient thus could be determined by free stream velocity u_∞, fluid temperature T_∞, wall temperature T_w, and wall position x on a flat plate, etc.

We define the local exergy transfer Nusselt number Nu_{ex} as follows:

$$Nu_{ex} = \frac{\alpha_{ex}x}{\lambda}. \quad (26)$$

Combining Eq. (26) with Eq. (24) leads to Nu_{ex} for laminar flow as

$$Nu_{ex,lam} = 0.332Re_x^{1/2}Pr^{1/3}(1 - T_0/T_\infty)$$
$$-[0.332Re_x^{5/2}\rho T_0 v^3]/[\lambda x^2 T_\infty(T_w - T_\infty)]. \tag{27}$$

Nu_{ex} can be obtained in non-dimensional form using non-dimensional variables defined as follows:

$$J = (\rho v^3)/(\lambda T_0 l^2), \tag{28a}$$

$$T_\infty^* = T_\infty/T_0, \tag{28b}$$

$$T_w^* = T_w/T_0, \tag{28c}$$

$$x^* = x/l, \tag{28d}$$

$$Re_l = u_\infty l/v. \tag{28e}$$

Thus, Eq. (27) may be rewritten as

$$Nu_{ex,lam} = 0.332(x^*)^{1/2}Re_l^{1/2}Pr^{1/3}(1 - 1/T_\infty^*)$$
$$-[0.332JRe_l^{5/2}(x^*)^{1/2}]/[T_\infty^*(T_w^* - T_\infty^*)]$$
$$= (Nu_{ex,\Delta T})_{lam} - (Nu_{ex,\Delta p})_{lam}. \tag{29}$$

Proceeding in a similar fashion, it is readily shown that Nu_{ex} for turbulent flow is

$$Nu_{ex,turb} = 0.0296(x^*)^{4/5}Re_l^{4/5}Pr^{1/3}(1 - 1/T_\infty^*)$$
$$-[0.0296JRe_l^{14/5}(x^*)^{4/5}]/[T_\infty^*(T_w^* - T_\infty^*)]$$
$$= (Nu_{ex,\Delta T})_{turb} - (Nu_{ex,\Delta p})_{turb}. \tag{30}$$

To further reflect the exergy rate transferred by external flow, the local non-dimensional exergy flux q_{ex}^* is defined as

$$q_{ex}^* = \frac{q_{ex}}{T_0(\lambda/l)} = \frac{\alpha_{ex}\Delta T}{T_0(\lambda/l)}. \tag{31}$$

Applying Eqs. (24), (25), and (31) for q_{ex}^* of laminar and turbulent flow, we have

$$q_{ex,lam}^* = \frac{q_{ex,lam}}{T_0(\lambda/l)} = 0.332 Re_l^{1/2} Pr^{1/3}(x^*)^{-1/2}(1 - 1/T_\infty^*)(T_w^* - T_\infty^*)$$

$$-0.332 J Re_l^{5/2}(x^*)^{-1/2}/T_\infty^*$$

$$= (q_{ex,\Delta T}^*)_{lam} - (q_{ex,\Delta p}^*)_{lam}, \tag{32}$$

$$q_{ex,turb}^* = \frac{q_{ex,turb}}{T_0(\lambda/l)} = 0.0296 Re_l^{4/5} Pr^{1/3}(x^*)^{-1/5}(1 - 1/T_\infty^*)(T_w^* - T_\infty^*)$$

$$-0.0296 J Re_l^{14/5}(x^*)^{-1/5}/T_\infty^*$$

$$= (q_{ex,\Delta T}^*)_{turb} - (q_{ex,\Delta p}^*)_{turb}. \tag{33}$$

3.2.   The mean exergy transfer Nusselt number and exergy flux

The mean exergy transfer coefficient can be obtained by integrating over the laminar region ($0 < x < x_c$) and then over the turbulent region ($x_c < x < l$); this equation may be expressed as

$$\alpha_{em} = \frac{1}{l} \left(\int_0^{x_c} \alpha_{ex,lam} dx + \int_{x_c}^l \alpha_{ex,turb} dx \right), \tag{34}$$

where it is assumed that transition occurs abruptly at $x = x_c$. Substituting from Eqs. (24) and (25) for α_{ex} of laminar flow and turbulent flow, respectively, we obtain

$$\alpha_{em} = \frac{\lambda}{l} \left\{ \begin{array}{l} [0.664 Re_c^{1/2} + 0.037(Re_l^{4/5} - Re_c^{4/5})] Pr^{1/3}(1 - 1/T_\infty^*) \\ -\dfrac{J[0.664 Re_c^{5/2} + 0.037((x_c^*)^2 Re_l^{14/5} - Re_c^{14/5})]}{(x_c^*)^2 T_\infty^*(T_w^* - T_\infty^*)} \end{array} \right\}, \tag{35}$$

where $x_c^* = x_c/l$ is the non-dimensional critical distance of a flat plate.

Thus, the mean exergy transfer Nusselt number over the entire flat plate (including laminar and turbulent flow regions) becomes

$$Nu_{em} = \alpha_{em} l/\lambda = [0.664 Re_c^{1/2} + 0.037(Re_l^{4/5} - Re_c^{4/5})] Pr^{1/3}(1 - 1/T_\infty^*)$$

$$-\frac{J[0.664 Re_c^{5/2} + 0.037((x_c^*)^2 Re_l^{14/5} - Re_c^{14/5})]}{(x_c^*)^2 T_\infty^*(T_w^* - T_\infty^*)}$$

$$= Nu_{em,\Delta T} - Nu_{em,\Delta p}. \tag{36}$$

Similarly, substituting from Eqs. (32) and (33), for q_{ex} of laminar flow and turbulent flow, respectively, it follows that the mean non-dimensional exergy flux over the entire flat plate is

$$q_{em}^* = \frac{q_{em}}{T_0(\lambda/l)} = [0.664Re_c^{1/2} + 0.037(Re_l^{4/5} - Re_c^{4/5})]Pr^{1/3}(1 - 1/T_\infty^*)$$

$$(T_w^* - T_\infty^*) - J[0.664Re_c^{5/2} + 0.037((x_c^*)^2 Re_l^{14/5} - Re_c^{14/5})]/[(x_c^*)^2 T_\infty^*]$$

$$= q_{em,\Delta T}^* - q_{em,\Delta p}^*. \tag{37}$$

For comparison, the non-dimensional heat fluxes over a flat plate are given by the following non-dimensional forms:

$$q_{x,lam}^* = \frac{q_x}{T_0(\lambda/l)} = 0.332Re_l^{1/2}Pr^{1/3}(x^*)^{-1/2}(T_w^* - T_\infty^*), \tag{38}$$

$$q_{x,turb}^* = \frac{q_x}{T_0(\lambda/l)} = 0.0296Re_l^{4/5}Pr^{1/3}(x^*)^{-1/5}(T_w^* - T_\infty^*), \tag{39}$$

$$q_m^* = \frac{q_m}{T_0(\lambda/l)}$$

$$= (T_w^* - T_\infty^*)[0.664Re_c^{1/2}Pr^{1/3} + 0.037Pr^{1/3}(Re_l^{4/5} - Re_c^{4/5})]. \tag{40}$$

It is noted that, in light of the above, Nu_{ex}, Nu_{em}, q_{ex}^*, and q_{em}^* are related to the non-dimensional parameters Re_l, Pr, J, T_w^*, T_∞^*, etc., and may be less than zero when Re_l, Pr, J, T_w^*, T_∞^*, etc., are beyond the change range, which has no significance in engineering and draws our attention to the fact that the noteworthy parameters such as the process parameters and configuration must be within the limits permitted by exergy transfer.

Finally, it is noted from Eqs. (29), (30), (32), (33), (36), and (37) that the non-dimensional exergy transfer performance parameters can be expressed as the difference between two parts, namely, the first term on the right-hand side in each equation represents the contribution of exergy transfer parameters associated with heat transfer caused by finite temperature difference, and the second term represents the contribution of exergy transfer parameters associated with flow caused by pressure drop. The expressions of each term under different conditions are summarized in Table 1. Therefore, it can be concluded that the flow geometric parameters and Reynolds number etc., which is due to the different effects of them on each part, may be selected in order to maximize the exergy utilization associated with a specific external convection process.

Table 1 The contribution of non-dimensional exergy transfer performance parameters associated with heat transfer and flow pressure drop.

	Laminar flow region (local value)	Turbulent flow region (local value)
$Nu_{ex,\Delta T}$	$0.332(x^*)^{1/2}Re_l^{1/2}Pr^{1/3}(1-1/T_\infty^*)$	$0.0296(x^*)^{4/5}Re_l^{4/5}Pr^{1/3}(1-1/T_\infty^*)$
$Nu_{ex,\Delta p}$	$[0.332JRe_l^{5/2}(x^*)^{1/2}]/[T_\infty^*(T_w^*-T_\infty^*)]$	$[0.0296JRe_l^{14/5}(x^*)^{4/5}]/[T_\infty^*(T_w^*-T_\infty^*)]$
$q_{ex,\Delta T}^*$	$0.332Re_l^{1/2}Pr^{1/3}(x^*)^{-1/2}(1-1/T_\infty^*)(T_w^*-T_\infty^*)$	$0.0296Re_l^{4/5}Pr^{1/3}(x^*)^{-1/5}(1-1/T_\infty^*)(T_w^*-T_\infty^*)$
$q_{ex,\Delta p}^*$	$0.332JRe_l^{5/2}(x^*)^{-1/2}/T_\infty^*$	$0.0296JRe_l^{14/5}(x^*)^{-1/5}/T_\infty^*$

	Entire flat plate (mean value)
$Nu_{em,\Delta T}$	$[0.664Re_c^{1/2}+0.037(Re_l^{4/5}-Re_c^{4/5})]Pr^{1/3}(1-1/T_\infty^*)$
$Nu_{em,\Delta p}$	$J[0.664Re_c^{5/2}+0.037((x_c^*)^2Re_l^{14/5}-Re_c^{14/5})]/[(x_c^*)^2T_\infty^*(T_w^*-T_\infty^*)]$
$q_{em,\Delta T}^*$	$[0.664Re_c^{1/2}+0.037(Re_l^{4/5}-Re_c^{4/5})]Pr^{1/3}(1-1/T_\infty^*)(T_w^*-T_\infty^*)$
$q_{em,\Delta p}^*$	$J[0.664Re_c^{5/2}+0.037((x_c^*)^2Re_l^{14/5}-Re_c^{14/5})]/[(x_c^*)^2T_\infty^*]$

4. Results and discussions

In order to demonstrate the effects of different parameters on exergy transfer characteristics of laminar and turbulent forced convection through external flow over a flat plate, air is selected for working fluid. The environmental temperature $T_0 = 298$ K and a representative transition Reynolds number $Re_c = 5 \times 10^5$ are assumed. The wall temperature of a flat plate keeps constant and air properties are evaluated by the film temperature $((T_w + T_\infty)/2)$.
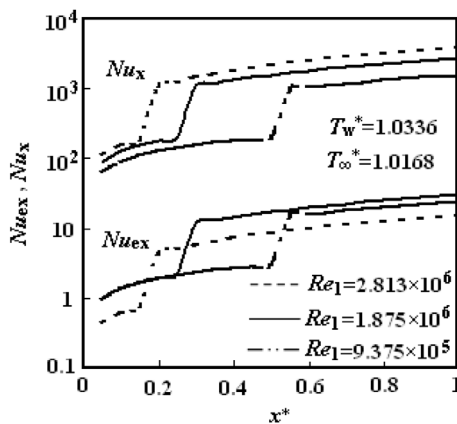
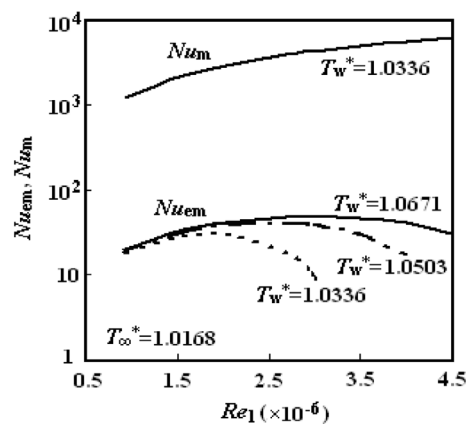**Figure 3** Variation of Nu_{ex} and Nu_x with x^* having Re_l as a parameter.

Figure 4 Variation of Nu_{em} and Nu_m with Re_l having T_w^* as a parameter.

Figure 3 represents the variations of Nu_{ex} and Nu_x with x^*, to illustrate the effect of the non-dimensional position over the entire length of the flat plat on exergy transfer performance. It is revealed from this figure that Nu_{ex} in both turbulent flow and laminar flow regions increases with x^* increment. However, Nu_{ex} in the turbulent flow region is greater than that in the laminar flow region, which indicates that exergy transfer performance in the turbulent flow region is superior to that in the laminar flow region. In this figure, the variation of Nu_x with x^* has been plotted as well, to facilitate a better comparison of x^* on exergy transfer and heat transfer performance through a flat plate. The results show that both Nu_{ex} and Nu_x increase with x^*, but Nu_{ex} is much less than Nu_x, which is due to the fact that only the quality of energy is considered in exergy transfer. Figure 4 shows the effects of Re_l on Nu_{em} and Nu_m over the entire length of a flat plate subjected to different T_w^*. This figure reveals that Nu_m increases with the increase of Re_l, whereas Nu_{em} increases first and then decreases with the increase of Re_l. So there exists an optimal Re_l to make Nu_{em} become maximal. Again, higher optimal Re_l values are obtained for higher T_w^* values. But the influence of T_w^* on Nu_m is slight, owing to the fact that the properties of air are slightly affected by the wall temperature of the flat plate. To investigate the effects of Re_l on $Nu_{em,\Delta T}$, $Nu_{em,\Delta p}$, and Nu_{em}, Figure 5 is furnished. This figure shows that Nu_{em} initially increases with an increase in Re_l; this is due to the fact that in this region, the increase in $Nu_{em,\Delta T}$ offsets more than the increase in $Nu_{em,\Delta p}$. However, as Re_l increases, $Nu_{em,\Delta p}$ eventually exceeds any increase in $Nu_{em,\Delta T}$ when beyond the optimal Re_l. The combined effect thus results in a maximum for Nu_{em} and the optimal Reynolds number corresponding to maximal Nu_{em} can be obtained.
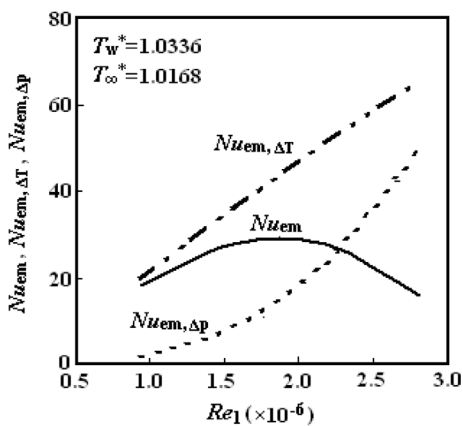

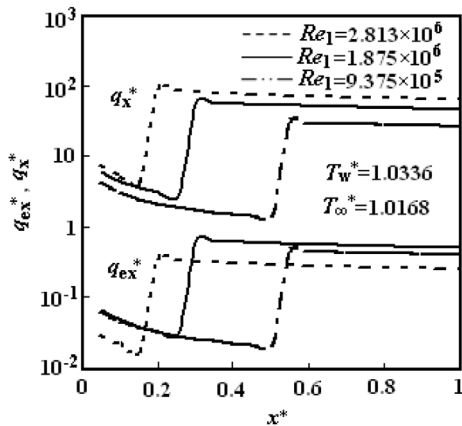**Figure 5** Variation of $Nu_{em,\Delta T}$, $Nu_{em,\Delta p}$ and Nu_{em} with Re_l.

Figure 6 Variation of q_{ex}^* and q_x^* with x^* having Re_l as a parameter.

To investigate the effects of x^* and Re_l on q_{ex}^* and q_x^*, Figure 6 is provided, which shows that q_{ex}^* in both turbulent flow and laminar flow regions decreases with x^* increment. However, q_{ex}^* in the turbulent flow region is greater than that in the laminar flow region, which further indicates that exergy transfer performance in the turbulent flow region is superior to that in the laminar flow region. Furthermore, q_{ex}^* is much less than q_x^*. From the numerical results, it is also noted that the trends of variations of $q_{ex,\Delta T}^*$, $q_{ex,\Delta p}^*$, and q_{ex}^* with x^* in the turbulent flow region are the same as those in the laminar flow region, but the magnitudes are different due to different exergy transfer performance. Figures 7 and 8 depict the effects of Re_l on q_{em}^*, $q_{em,\Delta T}^*$, $q_{em,\Delta p}^*$, and q_m^*. As can be seen, with the increase of Re_l, q_m^* increases, but q_{em}^* presents a peak. In addition, higher q_{em}^* and q_m^* are obtained for higher T_w^*, and higher optimal Re_l for the corresponding maximal q_{em}^* is obtained for higher T_w^*. The effects of Re_l on $q_{em,\Delta T}^*$, $q_{em,\Delta p}^*$, and q_{em}^* are given in Figure 8. Similar effects are observed as indicated in the previous $Nu_{em,\Delta T}$, $Nu_{em,\Delta p}$, and Nu_{em} for external flow over the entire flat plate.
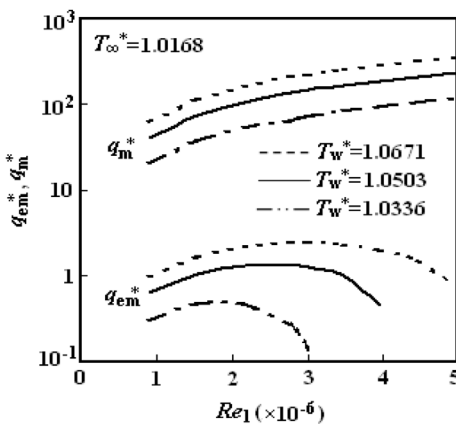
Figure 7   Variation of q_{em}^* and q_m^* with Re_l having T_w^* as a parameter.

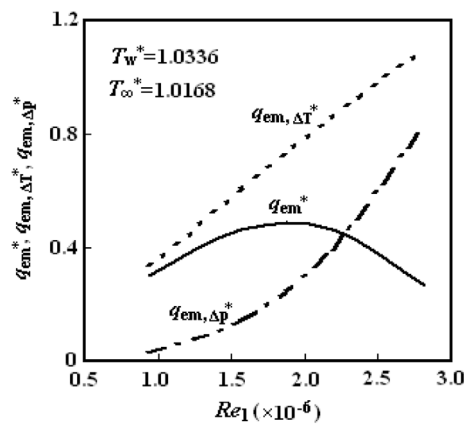**Figure 8**   Variation of $q_{em,\Delta T}^*$, $q_{em,\Delta p}^*$, and q_{em}^* with Re_l.

5.   Conclusions

The exergy transfer characteristics of external convection through a flat plate are examined on the basis of linear non-equilibrium thermodynamic theory. An analytical study has been carried out to investigate the influences of various geometric and operating parameters on the exergy transfer characteristics for laminar and turbulent flow over a flat plate subjected to a constant wall temperature. The local and mean exergy transfer Nusselt number and non-dimensional exergy flux are introduced, and a series of new generalized

expressions are derived. Air is selected as working fluid to illustrate their use and to demonstrate the effects of different parameters on the convective exergy transfer characteristics through external flow of a flat plate. It is found that the exergy transfer performance in the turbulent flow region is superior to that in the laminar flow region over a flat plate. Investigating the variation of exergy transfer performance with Reynolds number revealed that there is an optimum value for the Reynolds number for a given condition. In addition, the examined results has drawn our attention to the fact that those different benefits can be obtained by working fluids under different operating conditions and that noteworthy parameters such as the process parameters and the configuration parameters must be within the limits permitted by exergy transfer. On the other hand, for better perceiving the role of different parameters on exergy transfer performance, the corresponding results of energy transfer have been plotted as well. The results show that the exergy transfer characteristics are different from those of energy transfer. The present method thus permits an examination of exergy transfer characteristics in an external flow convection process. By maximizing the exergy transfer performance, a thermodynamic optimum can be determined for the operation of a given external flow convection process or in the selection of an enhancement heat transfer surface. The methods provided in this paper are also available for other forced convective heat transfer processes through external flow.

Nomenclature

A	heat (exergy) transfer area, m^2
c_p	specific heat capacity at constant pressure, J/kg K
C_f	friction coefficient
e	specific flow exergy of fluid, J/kg
E	exergy change rate, W
F_D	drag force, N
G_∞	mass flow rate, kg/s
h	specific enthalpy of fluid, J/kg
J	flow
L	phenomenological coefficient
l	length of flat plate along the direction of flow, m
Nu	heat transfer Nusselt number
Nu_e	exergy transfer Nusselt number
p	pressure, Pa
Pr	Prandtl number
q	heat flux, W/m^2
q_e	exergy flux, W/m^2

Re	Reynolds number
s	specific entropy of fluid, J/kg K
T	temperature, K
ΔT	temperature difference between wall and free stream, K
T_0	environmental temperature, K
T_w	wall temperature of flat plate, K
T_∞	temperature of free stream, K
u_∞	velocity of free stream, m/s
V_∞	volume flow rate, m^3/s
X	thermodynamic force
x	distance from the leading edge, m
x_c	distance from the leading edge at which transition begins, m

Greek symbols

α	convective heat transfer coefficient, W/m^2 K
α_e	convective exergy transfer (phenomenological) coefficient, W/m^2 K
ρ	density of fluid, kg/m^3
ν	kinematical viscosity coefficient of fluid, m^2/s
λ	thermal conductivity of fluid, W/m K
μ	potential
Φ	heat transfer rate, W
Φ_e	exergy transfer rate, W

Subscripts

0	environmental state
c	critical value
lam	laminar flow value
m	mean value
turb	turbulent flow value
x	local value
ΔT	contribution of exergy transfer parameters associated with heat transfer caused by finite temperature difference
Δp	contribution of exergy transfer parameters associated with flow caused by pressure drop

Superscripts

*	non-dimensional value

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On Diffusion and Permeation

Stephen S.L. Peppin
OCCAM, Mathematical Institute, Oxford University, OX1 3LB, UK

e-mail: peppin@maths.ox.ac.uk

Abstract

Diffusion and permeation are discussed within the context of irreversible thermodynamics. A new expression for the generalized Stokes–Einstein equation is obtained which links the permeability to the diffusivity of a two-component solution and contains the poroelastic Biot–Willis coefficient. The theory is illustrated by predicting the concentration and pressure profiles during the filtration of a protein solution. At low concentrations the proteins diffuse independently while at higher concentrations they form a nearly rigid porous glass through which the fluid permeates. The theoretically determined pressure drop is nonlinear in the diffusion regime and linear in the permeation regime, in quantitative agreement with experimental measurements.

1. Introduction

By observing the flow of water through a saturated column of sand, Darcy discovered an empirical constitutive relation between the volume flux of water and the drop in fluid pressure [8, 18]. Irreversible thermodynamics has been used to place several constitutive equations, such as Fick's and Fourier's laws, within a unified framework [10, 46]. Darcy's law has been somewhat exceptional in this endeavour as there have been a great number of different approaches used to incorporate the equation. For example, de Groot [9] treated a porous medium as a discontinuity between two fluid systems, leading to the membrane transport models of Katchalsky and coworkers [20, 21]. Vink modelled a rigid porous medium as a continuum by introducing a body force to account for the stress supported by the porous matrix [51]. A similar approach led to the Stefan–Maxwell theory of flow through porous media [25, 26]. Rational thermodynamicists derive constitutive relations using a non-equilibrium version of the second law as a constraint [5, 7, 35]. Later

workers have combined this approach with averaging methods [1, 15, 42, 56] to develop "hybrid" theories of flow through swelling porous media [2, 28].

Although much progress has been made, the fundamentals of flow through porous media are still uncertain, particularly in more complex cases such as swelling clays, colloidal solutions, and unsaturated systems [13, 14, 43]. It is interesting to note that Gibbs devoted a section of his treatise to the equilibrium thermodynamics of porous media [12]. He allowed the solid component to support non-hydrostatic stress, but otherwise modelled a porous medium as a single phase system, in close analogy with his treatment of fluids. In the present work diffusion and permeation are approached by treating a porous medium as a single thermodynamic phase. The main results are found to be consistent with previous ones, but allow for a closer connection to be made between chemical thermodynamics and poroelasticity. In particular, various poroelastic quantities such as the Biot–Willis and Skempton coefficients are defined thermodynamically, and limits are obtained on the relation between Fick's and Darcy's laws. The analysis begins in Section 2 with the mass and momentum balance equations of continuum mechanics and the hypothesis of local equilibrium. Gibbs's equilibrium thermodynamics is then utilized to evaluate the partial stress tensors. In Section 3 the equivalence of Fick's and Darcy's laws is demonstrated, leading to a Stokes–Einstein equation relating the diffusivity of a binary solution to the permeability, and containing the poroelastic Biot–Willis parameter. Two limiting exceptions to the equivalence, infinite dilution and infinite rigidity of the solute, are also discussed, and a relation between osmotic pressure and effective stress is obtained. The theory is utilized in Section 4 to study the ultrafiltration of a protein solution. There it is shown that at low concentrations the particles diffuse, while at higher concentrations they form a nearly rigid porous glass.

2.   Relative motion in two-component continua

The equations expressing balance of mass and momentum in the theory of interacting superposed continua have been given in quite general form by Truesdell [45, 46]. Here attention is restricted to isothermal two-component systems in which gravity is the sole body force and there are no chemical reactions. For convenience and without loss of generality component 1 is referred to as the solvent and component 2 the solute. Conservation of mass is expressed by the equations

$$\frac{\partial \rho}{\partial t} + \operatorname{div} \rho \mathbf{v} = 0, \quad \frac{\partial \rho_k}{\partial t} + \operatorname{div} \rho_k \mathbf{v}_k = 0, \tag{1}$$

where $\rho = \rho_1 + \rho_2$ is the local solution density (mass per unit volume), ρ_k is the partial density of component k, $\mathbf{v}$ is the mass-average velocity, and $\mathbf{v}_k$

is the local average velocity of k with respect to the laboratory frame, related to $\mathbf{v}$ by the equation $\rho\mathbf{v} = \rho_1\mathbf{v}_1 + \rho_2\mathbf{v}_2$.

Conservation of momentum can be written as

$$\rho\mathbf{a} = \operatorname{div}\mathbf{t} + \rho\mathbf{g} \tag{2}$$

for the solution and

$$\rho_k\mathbf{a}_k = \operatorname{div}\mathbf{t}_k + \rho_k\mathbf{g} + \mathbf{m}_k \tag{3}$$

for component k. Here $\mathbf{a}$ is the acceleration of the mean motion, $\mathbf{t}$ is the total stress tensor, and $\mathbf{g}$ is the acceleration due to gravity. The acceleration of component k is $\mathbf{a}_k$ and $\mathbf{t}_k$ is its partial stress tensor. The force $\mathbf{m}_1$, exerted on component 1 owing to its mean motion relative to component 2, can be written as [45]

$$\mathbf{m}_1 = f(\mathbf{v}_2 - \mathbf{v}_1), \tag{4}$$

where $\mathbf{v}_k$ is the average velocity of component k with respect to the laboratory frame and f is a coefficient of friction. In binary systems conservation of momentum requires that $\mathbf{m}_2 = -\mathbf{m}_1$ [45].

In his mechanical theory of diffusion, Truesdell [45] considers a mixture of ideal gases defined by the constitutive equations

$$\operatorname{div}\mathbf{t}_k = -\operatorname{grad}p_k, \quad \operatorname{div}\mathbf{t} = -\operatorname{grad}P, \tag{5}$$

where p_k is the partial pressure of k. Here his theory is extended to the case of a *hydrostatic solution* defined by the equations

$$\operatorname{div}\mathbf{t}_k = -\rho_k\operatorname{grad}\mu_k, \quad \operatorname{div}\mathbf{t} = -\operatorname{grad}P, \tag{6}$$

where μ_k is the chemical potential of component k, defined on a per unit mass basis, and P is the thermodynamic solution pressure. For an isothermal ideal gas mixture, Eq. (6) reduces to Eq. (5), since for an ideal gas $\mu_k = \mu_k^0(T) + R_kT \ln p_k$, where $p_k = \rho_k R_k T$ is the partial pressure of k, $R_k = R/M_k$, R is the gas constant, M_k is the molar volume of k, T is the absolute temperature, and μ_k^0 is a function of temperature only [34].

For a hydrostatic solution in the absence of accelerations and relative motion, Eqs. (2) and (3) combined with Eq. (6) reduce to the classic conditions for thermodynamic equilibrium obtained by Gibbs [12]:

$$\operatorname{grad}\mu_k = \mathbf{g}, \quad \operatorname{grad}P = \rho\mathbf{g}. \tag{7}$$

During irreversible processes the solution is assumed to be in local equilibrium [10]. Thus, at any point in the system the chemical potential μ_k and other thermodynamic quantities are determined, at constant temperature, by the local solution pressure P and partial density ρ_2. Thermodynamic quantities such as the chemical potential can be obtained from experiments on equilibrium systems, and retain the same functional dependence on the local values of P and ρ_2 at any point in the non-equilibrium system.

3. Equivalence of Fick's and Darcy's laws

In the absence of accelerations, Eqs. (2), (3), and (6) combine to give the following equations, which express conservation of momentum in an isothermal hydrostatic solution:

$$\rho_1 \operatorname{grad} \mu_1 = \rho_1 \mathbf{g} + f(\mathbf{v}_2 - \mathbf{v}_1), \tag{8}$$

$$\operatorname{grad} P = \rho \mathbf{g}. \tag{9}$$

It is convenient to introduce the *Darcy* pressure p as the pressure of the pure solvent component 1 when separated from an element of the solution by a semi-permeable partition. The osmotic pressure Π is then defined as the difference between the solution and Darcy pressures [16]:

$$\Pi = P - p. \tag{10}$$

Given the local equilibrium assumption, the solution on one side of the semi-permeable partition is at any given moment in equilibrium with the pure solvent on the other side. Hence the chemical potential μ_1 of component 1 in the solution is equal to the chemical potential μ_f of the pure solvent at pressure p:

$$\mu_1(T, P, \rho_2) = \mu_f(T, p). \tag{11}$$

Differentiating μ_f at constant temperature gives

$$\operatorname{grad} \mu_f = v_f \operatorname{grad} p, \tag{12}$$

where $v_f = (\partial \mu_f / \partial p)_T$ is the specific volume of pure solvent [16]. The Darcy pressure is an intensive thermodynamic variable which, at constant temperature and assuming local equilibrium, is a unique function of P and ρ_2. Therefore

$$\operatorname{grad} p = \left(\frac{\partial p}{\partial P} \right)_{T, \rho_2} \operatorname{grad} P + \left(\frac{\partial p}{\partial \rho_2} \right)_{T, P} \operatorname{grad} \rho_2. \tag{13}$$

Combining Eqs. (10)–(13) then gives

$$\text{grad}\mu_1 = \frac{v_f}{\alpha}\text{grad}P - v_f\left(\frac{\partial \Pi}{\partial \rho_2}\right)_{T,P}\text{grad}\rho_2, \tag{14}$$

where

$$\alpha = \left(\frac{\partial P}{\partial p}\right)_{T,\rho_2} \tag{15}$$

is the Biot–Willis parameter [4, 53, 54].

Combining Eqs. (8) and (9) with Eq. (14) and defining the diffusivity D and sedimentation coefficient s by

$$D = \frac{\rho_1^2 \rho_2 v_1 v_f}{f}\left(\frac{\partial \Pi}{\partial \rho_2}\right)_{T,P}, \quad s = \frac{\rho_1^2 v_1}{f}\left(\frac{\rho v_f}{\alpha} - 1\right) \tag{16}$$

leads to Fick's law:

$$\mathbf{J} = -D\text{grad}\rho_2 + \rho_2 s\mathbf{g}. \tag{17}$$

Here $\mathbf{J} = \rho_2(\mathbf{v}_2 - \mathbf{v}^0)$ is the mass flux of component 2 with respect to the volume-average velocity $\mathbf{v}^0 = \phi_1\mathbf{v}_1 + \phi_2\mathbf{v}_2$, with $\phi_k = \rho_k v_k$ the volume fraction and v_k the partial specific volume of component k. When the effect of gravity is negligible, Eq. (17) reduces to the more familiar form

$$\mathbf{J} = -D\text{grad}\rho_2. \tag{18}$$

Combining Eq. (8) with Eqs. (11) and (12), and defining the permeability $k = \rho_1^2 v_1 v_f \eta/f$, leads to Darcy's law:

$$\mathbf{q} = -\frac{k}{\eta}(\text{grad}p + \rho_f\mathbf{g}), \tag{19}$$

where η is the solvent viscosity, $\mathbf{q} = \phi_1(\mathbf{v}_1 - \mathbf{v}_2) = -\mathbf{J}/\rho_2$ is the volume flux of solvent relative to component 2, and $\rho_f = 1/v_f$ is the density of the pure solvent at pressure p. Equation (19), being equivalent to Eq. (17), shows that Darcy pressure gradients are responsible for diffusion in hydrostatic solutions. Truesdell [45] obtained a similar result for ideal gases, and the connection between Fick's and Darcy's laws has been demonstrated previously in soil science and colloid physics [23, 30, 31, 33, 40].

Eliminating f between the expressions for D and k gives

$$D = \rho_2\frac{k}{\eta}\left(\frac{\partial \Pi}{\partial \rho_2}\right)_{T,P}. \tag{20}$$

The generalized Stokes–Einstein relation (20) allows the diffusion coefficient to be calculated given measurements of the osmotic pressure and permeability. In many osmotic pressure experiments, however, it is not $(\partial\Pi/\partial\rho_2)_{T,P}$ that is measured but rather $(\partial\Pi/\partial\rho_2)_{T,p}$ [49]. That is, the pressure p of the pure solvent is held constant while the solution pressure P and partial density ρ_2 are varied. In this case, Eq. (20) can be written in the equivalent form

$$D = \frac{k}{\eta}\frac{K_\pi}{\alpha},\tag{21}$$

where $K_\pi = \rho_2(\partial\Pi/\partial\rho_2)_{T,p}$ is the osmotic bulk modulus and α is the Biot–Willis parameter introduced earlier. In the appendix it is shown that

$$\alpha = B^{-1}\left(1 - \frac{K_\pi}{K}\right),\tag{22}$$

where $K = \rho(\partial P/\partial\rho)_{T,c_2}$ is the bulk modulus of the solution, $c_2 = \rho_2/\rho$ is the solute mass fraction, and B is Skempton's coefficient [41, 53, 54]:

$$B = \left(\frac{\partial p}{\partial P}\right)_{T,c_2}.\tag{23}$$

With Eq. (11), the relations $v_1 = (\partial\mu_1/\partial P)_{T,c_2}$ and $v_f = (\partial\mu_f/\partial p)_T$ lead to a thermodynamic expression for Skempton's coefficient in terms of the solvent partial specific volume

$$B = \frac{v_1}{v_f}.\tag{24}$$

Interestingly, Eq. (24) indicates that in solutions with negative solvent partial specific volumes [38, 57] the Skempton coefficient is less than zero.

Eliminating f between the expressions for s and k gives

$$\frac{k}{\eta} = \frac{sv_f}{\rho v_f/\alpha - 1}.\tag{25}$$

With Eqs. (22) and (24), Eq. (25) becomes, to first order in K_π/K,

$$\frac{k}{\eta} = \frac{sB^{-1}}{\rho_2(1 - v_2/v_1) + \rho K_\pi/K},\tag{26}$$

where the relations $\rho = \rho_1 + \rho_2$ and $\rho_1 v_1 + \rho_2 v_2 = 1$ have been used. Equation (26) generalizes the relation between the permeability and sedimentation coefficient by accounting for the solvent compressibility. In dilute solutions

$K_\pi \ll K$ and $v_1 \approx v_f$, in which case Eq. (26) reduces to a form derived previously [10, 24, 26, 30]. Hence the Skempton and Biot–Willis coefficients have not traditionally been important parameters in irreversible thermodynamics. However, in solutions containing sufficiently rigid solutes that $K_\pi \sim K$ (e.g., colloidal glasses), it will be necessary to utilize Eqs. (21) and (26) when calculating D and k from osmotic pressure and sedimentation data.

The equivalence of Eqs. (17) and (19) breaks down in two limiting cases:

Infinite dilution – In the dilute limit $\rho_2 \to 0$ and $D \to D_0$, where D_0 is a constant. In this case $(\partial\Pi/\partial\rho_2)_{T,P}$ is constant and Eq. (20) yields $k \to \infty$. Therefore k is undefined and Darcy's law cannot be used to characterize infinitely dilute solutions.

Infinite rigidity – For an infinitely rigid solute, $K_\pi \to \infty$ and $k \to k_0$, where k_0 is a constant. In this case, Eq. (21) yields $D \to \infty$. Therefore D is undefined and Fick's law does not apply to binary solutions containing infinitely rigid solutes. In real systems the above limits are never met, and the equivalence of Fick's and Darcy's laws is quite general. Note that a rigid solute, defined by an infinite osmotic bulk modulus, is not equivalent to an incompressible solute, for which the partial specific volume v_2 is constant. If, in a particular system, v_2 is constant *and* K_π is infinite, then the solute is both incompressible and rigid. A solution containing a fluid solvent and a rigid incompressible solute provides a thermodynamic analogue of a rigid porous medium.

In order to solve particular problems it is necessary to know the functional dependence of Π on P and ρ_2. For dilute solutions $\Pi = \rho_2 RT/M_p$, where R is the gas constant and M_p is the solute molar mass [34]. In concentrated solutions and colloidal suspensions determining $\Pi(T, P, \rho_2)$ is a formidable task, which is often simplified by assuming constant T, P and determining $\Pi(\rho_2)$ experimentally. A different simplification is used in the case where the solute undergoes only small changes in concentration, such as a linearly elastic porous matrix [3, 36, 54]. Rearranging Eq. (13) gives

$$\mathrm{d}P = \frac{1}{\rho_2}K_\pi\,\mathrm{d}\rho_2 + \alpha\,\mathrm{d}p. \tag{27}$$

For small variations from an initial unstressed and depressurized state where $\rho_2 = \rho_2^0$, $P = 0$, and $p = 0$, Eq. (27) can be integrated to yield

$$\sigma' = K_\pi\epsilon, \tag{28}$$

where $\epsilon = (\rho_2^0 - \rho_2)/\rho_2$ is the volumetric strain of component 2 and

$$\sigma' = -P + \alpha p \tag{29}$$

is the effective stress. Thus, by defining an effective stress as a linear combination of the total stress $\sigma = -P$ and the Darcy pressure p, the equation describing the volumetric strain of component 2 takes on an identical form to that for a nonporous linearly elastic solid, and hence well-known solutions to problems in elasticity can be applied directly to problems involving porous media [29, 54]. With Eq. (10) the relation between osmotic pressure and effective stress is

$$\Pi = (\alpha - 1)p - \sigma' \tag{30}$$

or, for nonhydrostatic stress,

$$\mathbf{\Pi} = (\alpha - 1)p\mathbf{I} - \mathbf{\sigma}', \tag{31}$$

where $\mathbf{\Pi}$ and $\mathbf{\sigma}'$ are tensors and $\mathbf{I}$ is the unit tensor. If α is constant then Eq. (30) gives

$$\left(\frac{\partial \Pi}{\partial \rho_2}\right)_{T,p} = -\left(\frac{\partial \sigma'}{\partial \rho_2}\right)_{T,p}, \tag{32}$$

and knowledge of σ' can be used to determine the diffusivity in Eq. (21). In the case of solutions undergoing large changes in concentration, the effective stress concept is less useful and the dependence of Π on P and ρ_2 must be determined experimentally or using statistical thermodynamics [17].

4. Protein ultrafiltration

The theory described above can be illustrated by considering the ultrafiltration of a protein solution, such as bovine serum albumin (BSA). In steady-state dead-end ultrafiltration, a fixed mass of macromolecules is placed above a semi-permeable membrane; above the macromolecules is a solvent reservoir [19, 22, 52]. At $t = 0$ the solution pressure P is increased, forcing solvent to flow through the system. Similar processes occur in many biological and technological settings.

As BSA is a well-characterized protein, extensive measurements of the relevant transport coefficients for aqueous solutions are available. For the sedimentation coefficient s the experimental measurements of Comper et al. [6] and van den Berg et al. [47], shown in Figure 1a, can be fitted to the function

$$s = s_0 \left(1 + a\rho_2 + b\rho_2^2 + c\rho_2^3\right)^{-1}, \tag{33}$$

where $a = 1.2 \times 10^{-2}, b = 2.0 \times 10^{-5}, c = 9.6 \times 10^{-8}$, and $s_0 = 4.4 \times 10^{-13}$ s is the sedimentation coefficient in the dilute limit [47].
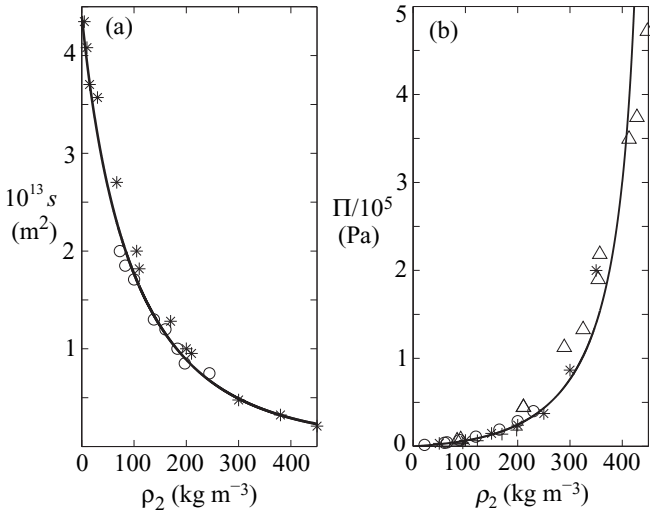
Figure 1 (a) Measurements of the sedimentation coefficient of BSA (pH 7.4) as a function of concentration (○ Comper et al. [6]; ∗ van den Berg et al. [47]). The solid curve is a fit of the data to Eq. (33). (b) Measurements of the osmotic pressure of BSA (pH 7.4) as a function of concentration (Δ Vilker et al. [49]; ∗ Kim et al. [22]; ○ Scatchard et al. [39]; + Comper et al. [6]). The solid curve is a fit of the data to Eq. (34) using $v_e = 1.38 \times 10^{-3}$ kg/m^3.
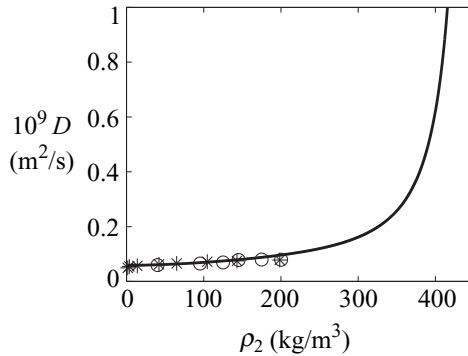
Figure 2 Measurements of the diffusion coefficient of BSA (pH 7.4) as a function of concentration (∗ Phillies et al. [32]; ○ Fair et al. [11]). The solid curve is the prediction of the generalized Stokes–Einstein equation.

Vilker et al. [49] measured the osmotic pressure of BSA (holding p constant), shown in Figure 1b. As noted by Minton [27], the osmotic pressure of BSA is well described by a hard sphere model with effective particle volume. The solid line in Figure 1b is a fit to the data using the equation

$$\Pi = \frac{RT}{M_p} \rho_2 Z_{HS}(\phi), \tag{34}$$

where R is the molar gas constant, $M_p = 69,000$ is the BSA molar mass, and Z_{HS} is the hard sphere compressibility factor [31,37], with $\phi = v_e \rho_2$ the volume fraction and v_e the effective particle specific volume.

Vilker [50] has shown that $v_1 \approx v_f$ up to $\rho_2 > 400\,\text{g/cm}^3$. Since $K_\pi \ll K$ over this range in ρ_2, Eqs. (21) and (26) may be utilized with $\alpha = 1$ and $B = 1$ to obtain $D(\rho_2)$. The predicted diffusivity is plotted on Figure 2, and compared with the experimental measurements of Phillies et al. [32] and Fair et al. [11], yielding good agreement. The osmotic pressure of BSA and many colloidal suspensions diverges at higher concentrations (Figure 1b), while the sedimentation coefficient approaches a constant (Figure 1a). Since the osmotic pressure diverges, the Stokes–Einstein equation ensures the diffusivity must also increase, as illustrated in Figure 2. As will be seen, the rapid increase of Π and D with ρ_2 at higher concentrations has a profound effect on the concentration and pressure profiles in ultrafiltration boundary layers [55].

At steady state in a dead-end ultrafiltration experiment, conservation of mass for the solvent becomes $\nabla \cdot \rho_1 \mathbf{v}_1 = 0$. Since v_1 is constant and $\mathbf{v}_2 = 0$ at steady state, this can be written as $\nabla \cdot \mathbf{q} = 0$. Hence the solvent volume flux is constant throughout the boundary layer. For a one-dimensional system,

$$\mathbf{q} = -\frac{Q}{A}\mathbf{k}, \tag{35}$$

where Q is a measured flow rate, A is the cross-sectional area of the membrane, and $\mathbf{k}$ is the unit normal to the membrane surface. Combining Eq. (35) with Darcy's law (19) and Fick's law (18) and neglecting gravity gives

$$\frac{Q}{A} = \frac{k}{\eta}\frac{dp}{dz} = -\frac{D}{\rho_2}\frac{d\rho_2}{dz}. \tag{36}$$

Given the mass m of protein molecules placed above the membrane, Eq. (36) can be integrated to obtain the concentration ρ_2^0 at the membrane surface as

$$\int_0^{\rho_2^0} D\,d\rho_2 = \frac{mQ}{A^2}. \tag{37}$$

With ρ_2^0, Eq. (36) then gives an initial value problem for $\rho_2(z)$, from which the Darcy pressure profile $p(z)$ can be obtained using Eqs. (10) and (34).

Wang [52] performed dead-end ultrafiltration experiments on BSA solutions (pH 7.4, $A = 3.88\,\text{cm}^2$, $m = 75\,\mu\text{g}$) in which the steady flow rates Q and Darcy pressure profiles $p(z)$ were measured at two different transmembrane pressures ($P = 2.7\,\text{kPa}$ and $P = 5.6\,\text{kPa}$). The flow resistance of the membrane in Wang's system was negligible compared to that of the polarization
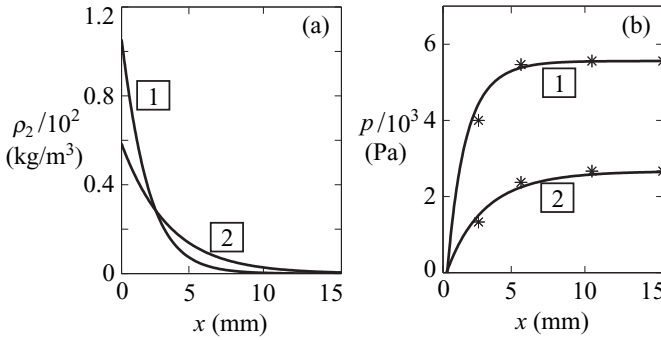
Figure 3 Concentration and Darcy pressure profiles during the dead-end ultrafiltration of BSA. Curves 1 and 2 correspond to steady-state flow rates of $Q = 13.3 \times 10^{-12}\,\mathrm{m^3/s}$ and $7.1 \times 10^{-12}\,\mathrm{m^3/s}$, respectively. Experimental data is from Wang [52] ($*$).
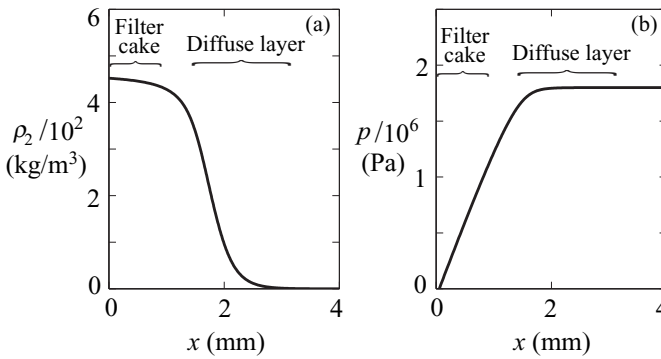
Figure 4 Predicted concentration and Darcy pressure profiles during high-pressure dead-end ultrafiltration of BSA.

layer [52]. The predicted concentration and pressure profiles from Eqs. (36) and (10) are shown in Figure 3, along with the experimental measurements. The Darcy pressure varies nonlinearly throughout the boundary layer (Figure 3b). From Figure 2 it is apparent that the diffusion coefficient is practically constant throughout the boundary layer, consistent with the exponential concentration profiles in Figure 3a.

It is interesting to consider higher pressures than used by Wang [52]. Figure 4 shows the predicted profiles of ρ_2 and p for $m = 3.0 \times 10^{-4}\,\mathrm{kg}$, $P = 1.85\,\mathrm{MPa}$, and $Q = 10^{-10}\,\mathrm{m^3/s}$. In this case the concentration profile is no longer exponential, and a glassy solid filter cake has formed against the membrane surface; the concentration is roughly constant within the cake. The explanation for this qualitatively different behaviour is found in Figure 2, which shows the diffusivity D diverging rapidly as the concentration increases. When D diverges the system adopts poroelastic behaviour, as discussed in Section 3 and

demonstrated by the linear pressure profile in the filter cake region (Figure 4b). In addition, a relatively small and nonlinear pressure drop occurs across the diffuse part of the boundary layer. For solution pressures in excess of 1 MPa, the pressure drop across the diffuse layer is negligible compared to that across the filter cake. This result is consistent with the measurements of Trettin and Doshi [44], who observed poroelastic behaviour during BSA ultrafiltration as the solution pressure approached 1 MPa ("gel limited" regime). It also explains the results of Vilker et al. [48], who attempted to detect the filter cake during dead-end filtration of BSA and found only exponential concentration profiles. The maximum transmembrane pressure used in their experiments was 276 kPa, well below that required to form an observable cake.

5. Acknowledgments

6. Appendix

Combining the identity

$$\left(\frac{\partial p}{\partial P}\right)_{T,\rho_2}\left(\frac{\partial P}{\partial \rho_2}\right)_{T,p}\left(\frac{\partial \rho_2}{\partial p}\right)_{T,P} = -1 \tag{38}$$

with Eqs. (15) and (10) yields

$$\left(\frac{\partial \Pi}{\partial \rho_2}\right)_{T,P} = \frac{K_\pi}{\rho_2 \alpha}, \tag{39}$$

where $K_\pi = \rho_2(\partial \Pi/\partial \rho_2)_{T,p}$. Combining Eq. (39) with Eq. (20) gives Eq. (21). Defining the solute mass fraction $c_2 = \rho_2/\rho$, the identity

$$\left(\frac{\partial p}{\partial P}\right)_{T,c_2} = \left(\frac{\partial p}{\partial P}\right)_{T,\rho_2} + \left(\frac{\partial p}{\partial \rho_2}\right)_{T,P}\left(\frac{\partial \rho_2}{\partial P}\right)_{T,c_2} \tag{40}$$

combined with Eqs. (38), (15), and (10) gives Eq. (22).

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Non-Equilibrium Thermodynamics of Gene Expression and Transcriptional Regulation

Enrique Hernández Lemus [1,2]
[1] Department of Computational Genomics,
National Institute of Genomic Medicine,
Periférico Sur No. 4124, Torre Zafiro II, Piso 5,
Col. Ex Rancho de Anzaldo, Álvaro Obregón 01900, México, D.F. México
[2] Center for the Sciences of Complexity,
Universidad Nacional Autónoma de México,
Torre de Ingeniería, Piso 6, Circuito Escolar s/n,
Ciudad Universitaria, Coyoacán, 04510, México, D.F. México

e-mail: ehernandez@inmegen.gob.mx

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Abstract

In recent times whole-genome gene expression analysis has turned out to be a highly important tool to study the coordinated function of a very large number of genes within their corresponding cellular environment, especially in relation to phenotypic diversity and disease. A wide variety of methods of quantitative analysis has been developed to cope with high throughput data sets generated by gene expression profiling experiments. Due to the complexity associated with *transcriptomics*, especially in the case of gene regulation phenomena, most of these methods are of a probabilistic or statistical nature. Even if these methods have reached a central status in the development of an integrative, systematic understanding of the associated biological processes, they very rarely constitute a concrete guide to the actual physicochemical mechanisms behind biological function, and the role of these methods is more on a hypotheses generating line. An important improvement could lie in the development of a thermodynamic theory for gene expression and transcriptional regulation that will build the foundations for a proper integration of the vast amount of molecular biophysical data and could lead, in the future, to a systemic view of genetic transcription and regulation.

1. Introduction

Cellular phenotypes are mainly determined by the expression levels of many genes and their products such as enzymes, proteins and so on. One important tool to track down this cellular phenotypic diversity is gene expression analysis. One hard-to-grasp issue is that the process of gene expression in itself is a complex one, both from the biochemical and thermodynamical points of view [1]. The transcription of messenger RNA (mRNA) for a given gene from a DNA template often is regulated by different genes and their products. This being the case, a variety of physicochemical interactions abounds between genetic transcript abundance, and it is a recognized fact that such complex processes are behind the ultimate mechanisms of cell function. Under this scenario, gene expression values are measured under different conditions, either on a simultaneous [steady-state] or serial [dynamics] fashion; in many cases the measurements are then treated as samples from a joint probability distribution. Genome-wide transcriptional profiling, also called gene expression analysis (GEA) has allowed us to go well beyond studying gene expression at the level of individual components of a given process by providing global information about functional connections between genes, mRNAs, and the related regulatory proteins. GEA have greatly increased our understanding of the interplay between different events in gene regulation and have pointed out previously unappreciated biological functional relations, such as the coupling between nuclear and cytoplasmic transcription and metabolic processes [2]. GEA has also revealed extensive communication within regulatory units, for example in the organization of transcription factors into regulatory motifs.

The transcriptional behavior for every gene is simultaneously regulated by both its related chromatin structure and associated transcription factors. In eukaryotes (organisms with a cellular nucleus), for example, genomic DNA is packaged into nucleosomes that are made of DNA and octamers of a class of proteins called *histones*. Another set of proteins called *chromatin modifiers* are able to move the histones all along the DNA chain to expose specific regions and then replace histones with *specific histone variants* to convert chromatin from a transcriptionally repressed state into a transcriptionally accessible state, hence enabling gene expression. In the case of transcription factors (TFs), they bind at regulatory regions to either activate or repress the transcription of their *target genes*. TFs do this by (respectively) promoting or inhibiting recruitment of RNA polymerase II. Transcription factors (TFs) also recruit chromatin-modifying enzymes to make their target DNA more accessible to the *transcriptional machinery* (for a more detailed account, see Section 3). In the past, the different steps involved in the regulation of gene expression – transcription, mRNA processing, nuclear export, translation and degradation – were usually analyzed *in isolation* by using conventional bio-

chemical techniques. This way of looking at things has given the impression that such processes are independent. Former investigations were focused on the mechanisms underlying individual gene expression, or in the best scenario, the behavior of a small set of genes, rather than exploring regulatory mechanisms that can influence many genes at one time. Systematic studies of genome-wide binding patterns made evident the existence of a great deal of coordinated regulation among TFs. Factors that combinatorialy regulate (in a concomitant way) a particular gene also often coordinately regulate the expression of other genes, potentially even themselves or each other. Given this fact, they are not independent inputs that merge only at a particular promoter, but rather are coupled. Of course, these complex phenomena will ultimately affect a thermodynamical description of transcription regulation because the concentrations (expression levels) and chemical potentials of mRNA transcripts are combinatorialy correlated.

Nevertheless, even if we are now provided with experimental techniques to measure the behavior of thousands of mRNA transcripts simultaneously, and a great deal of attention has been put on the computational and statistical analysis of such huge amounts of data, the theoretical approach is still looking at the regulatory interactions on a one by one basis. This approach is of course changing toward a more systematic, network-oriented understanding of gene regulation phenomena. One usual means to understand the nature of such intricate phenomena is by using the so-called gene regulatory networks (GRNs). GRNs are powerful graph-theoretical constructs that describe the integrated status of a cell under a specific condition at a given time [3]. The complex description given by GRNs consists, generally, in identifying gene interactions from experimental data through the use of theoretical models and computational analysis [4]. Transcriptional network analyses have showed that, instead of being independent, different levels of gene regulation are strongly coupled. In some cases, it has been recognized that the factors involved in a specific stage of mRNA transcription can exhibit coordinated behavior, for example, by finding how groups of transcription factors bind cooperatively at many related promoters.

2. Thermodynamics of hybridization

Understanding the thermodynamical basis of the hybridization process is an important task related to both the explicit, intrinsic mechanisms of gene expression and its experimental measurement, especially in the case of high throughput technologies such as the gene chips. One initial approach is to calculate hybridization thermodynamics based on the inference of free energies by means of the energetic cost of base-pair opening in the RNA com-

plex [5]. This approach has also been applied to understanding the selective hybridization processes related to mRNA silencing (gene switching) by means of small interfering RNA molecules (siRNAs), which are RNA molecules that bind (hybridize) to specific mRNA transcripts, thus forbidding their ultimate translation into proteins [6]. In both scenarios, the thermodynamic equilibrium and its properties are important for understanding and quantifying the degree of hybridization, the specificity of it, and the steady-state concentration of mRNA transcripts after either the measurement process or the silencing, respectively. In the present paper, we are more interested in the thermodynamics associated with gene expression quantification and profiling in high throughput experiments, since this is (at least at the moment) the ultimate and more accurate laboratory tool for studying the mechanism of genetic transcription.

According to the Langmuir adsorption model of oligonucleotide hybridization, the specific-hybridization intensity (or gene expression signal) for a gene probe as measured by (for example) an Affymetrix-type gene chip [7] is given by [5]

$$\varphi(c, \Delta G) = \frac{A \, c \, e^{-\beta \Delta G}}{1 + c \, e^{-\beta \Delta G}}, \tag{1}$$

where $\beta = \frac{1}{RT}$, T is the local temperature, R is the gas constant, c is the mRNA concentration for this species, ΔG is the free energy of hybridization, and A is a parameter that sets the scale of the intensity corresponding to the saturation limit $c \gg e^{\beta \Delta G}$. A natural generalization of Eq. (1) for a probe i within a set of M gene-probes ($i = 1, \ldots, M$) is

$$\varphi_i(c_i, \Delta G_i) = \frac{A_i \, c_i \, e^{-\beta \Delta G_i}}{1 + c_i \, e^{-\beta \Delta G_i}}. \tag{2}$$

The local chemical potential μ_i of species i due to the hybridization process is defined customarily by $\mu_i = \left(\frac{\partial \Delta G_i}{\partial c_i} \right)_{T,P,c_j}$. From Eq. (2) it is possible to calculate μ_i by means of the chain-rule as follows:

$$\mu_i = \left(\frac{\partial \Delta G_i}{\partial c_i} \right)_{T,P,c_j} = \left(\frac{\partial \Delta G_i}{\partial \varphi_i} \right)_{T,P,c_j} \left(\frac{\partial \varphi_i}{\partial c_i} \right)_{T,P,c_j}, \tag{3}$$

or in terms of the direct derivatives:

$$\mu_i = \frac{\left(\frac{\partial \varphi_i}{\partial c_i} \right)_{T,P,c_j}}{\left(\frac{\partial \varphi_i}{\partial \Delta G_i} \right)_{T,P,c_j}}. \tag{4}$$

The first derivative is calculated as

$$\left(\frac{\partial \varphi_i}{\partial c_i} \right)_{T,P,c_j} = A_i \, c_i \, e^{-\beta \Delta G_i} \times \frac{-e^{-\beta \Delta G_i}}{(1 + c_i \, e^{-\beta \Delta G_i})^2}$$
$$+ \frac{1}{(1 + c_i \, e^{-\beta \Delta G_i})} \times A_i \, e^{-\beta \Delta G_i}. \quad (5)$$

If we re-arrange terms, we have

$$\left(\frac{\partial \varphi_i}{\partial c_i} \right)_{T,P,c_j} = \frac{A_i \, e^{-\beta \Delta G_i}}{(1 + c_i \, e^{-\beta \Delta G_i})} \times \left[1 - \frac{c_i \, e^{-\beta \Delta G_i}}{1 + c_i \, e^{-\beta \Delta G_i}} \right], \quad (6)$$

which can then be expressed in terms of φ_i to read

$$\left(\frac{\partial \varphi_i}{\partial c_i} \right)_{T,P,c_j} = \frac{\varphi_i}{c_i} \left[1 - \frac{\varphi_i}{A_i} \right]. \quad (7)$$

Now, in the case of the second derivative in Eq. (4), it is given by

$$\left(\frac{\partial \varphi_i}{\partial \Delta G_i} \right)_{T,P,c_j} = A_i \, c_i \, e^{-\beta \Delta G_i} \times \left[\frac{-c_i \, e^{-\beta \Delta G_i}(-\beta)}{(1 + c_i e^{-\beta \Delta G_i})^2} \right]$$
$$+ \frac{1}{(1 + c_i \, e^{-\beta \Delta G_i})} \times \left[A_i \, c_i \, e^{-\beta \Delta G_i}(-\beta) \right], \quad (8)$$

which then simplifies to

$$\left(\frac{\partial \varphi_i}{\partial \Delta G_i} \right)_{T,P,c_j} = \frac{A_i \, c_i^2 \, \beta \, e^{-2\beta \Delta G_i}}{(1 + c_i \, e^{-\beta \Delta G_i})^2} - \frac{A_i \, c_i \, \beta \, e^{-\beta \Delta G_i}}{1 + c_i \, e^{-\beta \Delta G_i}}. \quad (9)$$

Equation (9) could also be written in terms of φ_i:

$$\left(\frac{\partial \varphi_i}{\partial \Delta G_i} \right)_{T,P,c_j} = \frac{\beta \, \varphi_i^2}{A_i} - \beta \varphi_i, \quad (10)$$

which gives as a result that

$$\left(\frac{\partial \varphi_i}{\partial \Delta G_i} \right)_{T,P,c_j} = \beta \varphi_i \left[\frac{\varphi_i}{A_i} - 1 \right], \quad (11)$$

recalling Eqs. (4), (7), and (11), we finally get

$$\mu_i = \frac{\frac{\varphi_i}{c_i} \left(1 - \frac{\varphi_i}{A_i} \right)}{\beta \varphi_i \left(\frac{\varphi_i}{A_i} - 1 \right)} = \frac{-1}{\beta \, c_i} \quad (12)$$

or

$$\mu_i = \frac{-RT}{c_i}.$$ (13)

It is interesting to notice that this level of description (two-state Langmuir adsorption model) gives an expression (Eq. [13]) for the chemical potential that is equivalent to that of an *ideal gas*, i.e. non-interacting species, for if we calculate the equilibrium *chemical-work* contribution to the free energy, Ξ_i, we obtain

$$\Xi_i = \int \mu_i \, dc_i = \int \frac{-RT}{c_i} \, dc_i$$ (14)

or

$$\Xi_i = -RT \, ln\left(\frac{c_i}{c_i^o}\right).$$ (15)

This approximation is valid as long as the rate of *cross-hybridized targets* stays low, since if there is only (or mostly) *transcript-specific hybridization*, the chemical species (in this case the different mRNA molecules) could be considered non-interacting. This is a realistic assumption given the low concentrations of every transcript in solution and also the fact that current technologies are very efficient at reducing the rate of unspecific hybridization [7].

3.   Transcriptional regulation

The phenomenon of gene expression (also known as mRNA transcription or simply transcription) is a complex one. There is a set of control mechanisms collectively called *transcriptional regulation* that takes on the duty of controlling *when* transcription occurs and also *how much* mRNA is created. The transcription of a given gene by means of the RNA polymerase enzyme (RNApol) can be regulated or controlled by at least five different biochemical mechanisms.

- There exists a set of proteins called *specificity factors* that alter the specific binding of RNApol to some given *promoter* or set of *promoters*. A promoter is a DNA region located next – technically in the upstream cys location or toward the 5' region of the sense strand – to a gene that facilitates its transcription by making that region easy to recognize by the transcriptional machinery.

- *Repressors* are DNA-binding proteins whose function is the regulation of the expression of one or more genes by decreasing the rate of transcription.

The actual mechanism involves their attachment to an *operator*, hence forbidding the transcription of the adjacent segment of DNA by blocking the pass of RNApol.

- *Transcription factors* are proteins that bind to specific DNA sequences in order to control the rate of transcription. Transcription factors are able to perform their function alone, or by forming a complex with other proteins. Transcription factors bind to either enhancer or promoter regions of DNA adjacent to the genes that they regulate. Depending on the transcription factor, the transcription of the adjacent gene is either up- (i.e., higher concentrations of the corresponding mRNA) or down-regulated (lower concentrations of mRNA). Transcription factors use a variety of mechanisms for the regulation of gene expression. These mechanisms include stabilizing or blocking the binding of RNApol to DNA, catalyzing the acylation or deacylation of DNA. The transcription factor can either do this alone or by recruiting other proteins that possess catalytic activity.

- The DNA-binding proteins that enhance the interaction of RNApol to a particular promoter region, thus enlarging the expression levels of the associated gene, are called *activators*. Activators perform their work by means of either electrostatic interactions with some sub-units of RNApol (attracting the molecule toward them and hence toward the DNA region they are bound to) or by inducing conformational changes in the structure of DNA that facilitate its binding to RNApol.

- Finally, *enhancers* are regions in DNA that are able to be bound with activators, hence bringing promoters to the initiation complex.

4. Non-equilibrium thermodynamics for small reactive systems: The transcriptional regulation scenario

As is already evident from the previous section, the process of gene regulation within a cell is highly complex from the bio-physicochemical point of view. Another source of complexity in the non-equilibrium thermodynamical characterization of such a system lies in the fact that a cell is a *small system*, in the sense that its dimensions do not permit an obvious application of the thermodynamic limit. Specifically, the role of fluctuations and stochasticity within such scenarios is not clear. Small systems thermodynamics for equilibrium systems has been studied in the past [11, 12] and some results were even expected to extend to local equilibrium settings within cellular sized biosystems [13]. One important limitation for the development of such theoretical frameworks at that time was the lack of proper experimental settings to test their hypotheses. Nevertheless, with the development of modern techniques

such as microscopic manipulation by means of atomic force microscopes, optical tweezers and cold-traps, this situation has become less of a limitation. In the meantime, theories have been developed to explain several results. These include mesoscopic thermodynamical approaches [14, 19] and also studies made by means of the so-called fluctuation theorems [20–22, 24]. Fluctuation thorems have also been mentioned in connection with gene-transcription processes [23]. Some of these theoretical results have even been experimentally tested.

4.1. Fluctuation phenomena in non-equilibrium systems

To get a better idea of the role of large local fluctuations in small systems, let us recall an ideal gas composed of N particles. The total energy of the system is a Gaussian distributed random variable with average $< \epsilon > \sim N k_B T$ and variance $\sigma_\epsilon^2 \sim N k_B^2 T^2$. In that (general) case, the fluctuations of the system are proportional to $N^{-\frac{1}{2}}$. This means that for systems of size $N \approx \mathcal{O}[1]$ they are comparable (and thus important!), whereas for a system with $N \approx \mathcal{O}[10^{23}]$, these same fluctuations become negligible. An interesting case of study is the cell behavior of the RNApol molecule already mentioned. As we have said, RNApol is an enzyme that moves along the DNA to produce a newly synthesized mRNA molecule. It has been mentioned that RNApol extracts energy from its surrounding thermal bath (i.e., the cellular environment) to move, and at the same time uses bond hydrolysis to insure that only thermal fluctuations that lead to *forward* movement are captured. RNApol then serves as an out-of-equilibrium thermal rectifier. The complex dynamics behind even this (relatively) simple model of transcription demonstrate the necessity for a non-equilibrium thermodynamical characterization that includes the possibility to deal with fluctuations in small systems.

A very important concept in the non-equilibrium fluctuations setting is that of a *control parameter*. Roughly speaking, a control parameter is a variable that must be specified to define in an unambiguous manner the state of a non-equilibrium system, i.e., control parameters are non-fluctuating variables. Let us call x_n ($n = 1 \dots p$) the set of parameters of a non-equilibrium system and x_γ the control parameter. If we vary x_γ, then the total energy of the system will vary accordingly as

$$dU = \sum_{n \neq \gamma} \left(\frac{\partial U}{\partial x_n} \right)_{x_\gamma} dx_n + \left(\frac{\partial U}{\partial x_\gamma} \right)_{x_n} dx_\gamma. \tag{16}$$

One can see that the first term(s) correspond to the variation of energy as a result of internal configurations (we naïvely call this the *heat*), whereas

the second term is the energy change due to an external perturbation (that is the *work*). Of course, this formulation implies the experimental difficulty of finding an appropriate (natural) control parameter without disturbing (too much) the system. However, since there is a presence of thermal rectification phenomena in non-equilibrium small systems, Eq. (16) will serve as a basis for the extended irreversible thermodynamical description below.

4.2.   Mesoscopic non-equilibrium thermodynamics

As has already been said, systems outside the realms of the thermodynamic limit are characterized by large fluctuations and hence stochastic effects. The classic thermodynamic theory of irreversible process (CIT) [10] gives a rough, *coarse grained* description of the systems, one that ignores all the details of the molecular nature of matter, hence studying it as a continuum media by means of a phenomenological field theory. As such, CIT is not suitable for the description of small systems because fluctuations ignored by CIT could become the dominant factor in the system's dynamical evolution and response. Nevertheless, in many instances (such as the present case of gene expression regulation), it would be desirable to have a thermodynamic theoretical framework to study such so-called *nano-systems*. One possible way to do so is by considering the stochastic nature of the time evolution of small non-equilibrium systems. This is the approach followed by mesoscopic non-equilibrium thermodynamics (MNET) [14–16]. MNET for small systems could be understood as an extension of the equilibrium thermodynamics of small systems developed by Hill and co-workers [11–13].

The way in which stochasticity is coming into play is by means of recognizing that scaling down the description of a physical system brings up energy contributions that are usually neglected in thermodynamical descriptions either in equilibrium or outside of it. These contributions take the form of, for example, surface energies and bring in turn a disruption of the canonical view of extensivity. An example used by Hill [12] is that of a small cluster of N identical particles for which the equilibrium Gibbs energy is given as: $G = \mu N + a N^{\beta}$ with μ the chemical potential, a an arbitrary adjusting function, and $\beta < 1$ a *size-effect* exponent. Here, the second term represents these energies that are usually disregarded whose effects become negligible for very large N since the first term becomes dominant. In this way, at the thermodynamic limit one gets the usual $G = \mu N$ relation. It is then possible to treat the Gibbs energy as a fluctuating quantity. Of course we can *adjust* the definition of the chemical potential to account for these effects.

Defining

$$\widehat{\mu} = \mu + aN^{\beta-1}, \tag{17}$$

it is possible to recover the standard Euler relation $G = \widehat{\mu}N$. However, one must be cautious since even if $\widehat{\mu}$ accounts for the actual energy potential involved in the thermochemical description of such a small system, it is NOT a canonical chemical potential, since for instance, it does not a give rise to an extensive thermodynamical description. Of course in the thermodynamic limit $\widehat{\mu} \to \mu$.

In the same order of ideas, MNET was developed to characterize non-equilibrium small systems. Let us recall that any reduction of the spatio-temporal scale description of a system would entail an increase in the number of non-coarse grained degrees of freedom (we are *looking* at things with more detail so to speak). These degrees of freedom could be related with the extended variables in extended irreversible thermodynamics [27], but they could also be more microscopic in nature, such as colloidal-particle velocities, orientational states on a quasi-crystal, and so on. Hence, in order to characterize such variables, let us say that there exist a set $\Upsilon = \{v_i\}$ of such non-equilibrated degrees of freedom. $P(\Upsilon, t)$ is the probability that the system is at a state given by Υ at time t. If one assumes [15, 17] that the evolution of the degrees of freedom could be described as a diffusion process in Υ-space, then the corresponding Gibbs equation could be written as

$$\delta S = -\frac{1}{T} \int \mu(\Upsilon)P(\Upsilon, t)d\Upsilon. \tag{18}$$

$\mu(\Upsilon)$ is a generalized chemical potential related to the probability density, whose time-dependent expression could be explicitly written as

$$\mu(\Upsilon, t) = k_B T \, ln\frac{P(\Upsilon, t)}{P(\Upsilon)_{equil}} + \mu_{equil}, \tag{19}$$

or, in terms of a *nonequilibrium work term* ΔW,

$$\mu(\Upsilon, t) = k_B T \, lnP(\Upsilon, t) + \Delta W. \tag{20}$$

The time evolution of the system could be described as a generalized diffusion process over a potential landscape in the space of mesoscopic variables Υ. This process is driven by a generalized mesoscopic-thermodynamic force $\frac{\partial}{d\Upsilon}(\frac{\mu}{T})$ whose explicit stochastic origin could be tracked back by means of a Fokker–Planck-like analysis [14, 16, 17]. MNET seems to be a good candidate theory for describing non-equilibrium thermodynamics for small systems. In fact, the aforementioned arguments point to MNET being a good choice, *provided one*

has a suitable model or microscopic means to infer the probability distribution $P(\Upsilon, t)$.

One important setting where MNET seems appropriate is the case of activated processes, like a system crossing a potential barrier. Chemical reactions (and biochemical reactions like the ones involved in gene regulation too!) are clear in this case. According to [17] the diffusion current in this Υ-space could be written in terms of a local fugacity defined as

$$z(\Upsilon) = \exp \frac{\mu(\Upsilon)}{k_B T}, \tag{21}$$

and the expression for the associated flux will be

$$J = -k_B L \frac{1}{z} \frac{\partial z}{\partial \Upsilon}. \tag{22}$$

L is an Onsager-like coefficient. After defining a *diffusion coefficient D* and the associated affinity $A = \mu_2 - \mu_1$, the integrated rate is given as

$$\overline{J} = J_o \left(1 - \exp \frac{A}{k_B T} \right), \tag{23}$$

with $J_o = D \exp \frac{\mu_1}{k_B T}$.

One is then able to see that MNET gives rise to nonlinear kinetic laws like Eq. (23). In this context, MNET has been applied successfully in the past in biomolecular processes at (or under) the cellular level or description [18]. In that scenario, non-linear kinetics are used to express, for example, RNA unfolding rates as *diffusion currents*, modeled via transition state theory, giving rise to Arrhenius-type non-linear equations. In that case, the current was proportional to the chemical potential difference (cf. equation 17 of reference [18]), so the entropy production was quadratic in that chemical potential gradient. We will re-examine these kind of dependency later when discussing gene expression kinetics.

Since the whole-genome transcriptional regulation process consists of a (huge) series of biochemical reactions, and many of these have unexplored chemical kinetics, a detailed MNET analysis such as the one described above is unattainable at the present moment. In what follows, we will explore a phenomenologically based approach that nevertheless takes into account (although in a more intuitive, less explicit way) similar considerations as the MNET framework already sketched. This phenomenological approach is based on the extended irreversible thermodynamics assumption of enlargement of the thermodynamical variables space [25, 26].

4.3. Extended irreversible thermodynamics

We shall start our discussion by assuming that a generalized entropy-like function Ψ exists, which may be written in the form [27, 28]

$$\frac{d\Psi}{dt} = T^{-1}\left[\frac{dU}{dt} + p\frac{dv}{dt} - \sum_i \mu_i\frac{dC_i}{dt} - \sum_j \mathcal{X}_j \odot \frac{d\Phi_j}{dt}\right], \tag{24}$$

or as a differential form:

$$d_t\Psi = T^{-1}\left[d_t U + pd_t v - \sum_i \mu_i d_t C_i - \sum_j \mathcal{X}_j \odot d_t\Phi_j\right]. \tag{25}$$

We see that Eq. (25) is nothing but the formal extension of the celebrated Gibbs equation of equilibrium thermodynamics for the case of a multi-component out-of-equilibrium system. The quantities appearing therein are the usual ones: T is the local temperature, p and V the pressure and volume, etc. X_j and Φ_j are extended thermodynamical fluxes and forces. These extended forces and fluxes are the new elements of EIT, the ones that take into account the aforementioned non-local effects.

In the case of a multicomponent mRNA mixture at fixed volume and pressure, we will take our set of relevant variables to consist in the temperature $T(\vec{r}, t)$ and concentration of each gene species $C_i(\vec{r}, t)$ as the slow varying (classical) parameters set $\mathcal{S}$ and the *mass flux* of these species $\vec{J}_i(\vec{r}, t)$ as fast variables on the extended set $\mathcal{F}$ so that $\mathcal{G} = \mathcal{S} \bigcup \mathcal{F}$. These latter variables will take into account the presence of inhomogeneous regions (concentration domains formed because of the gene regulatory interactions) and so will correct the predictions based on the local equilibrium hypothesis. The non-equilibrium Gibbs free energy for a mixture of $i = 1 \ldots M$, mRNA transcripts at constant pressure, then reads

$$d_t G = -\Psi d_t T + \sum_i \mu_i d_t C_i + \sum_j \mathcal{X}_j \odot d_t\Phi_j. \tag{26}$$

If one is to consider gene expression/regulation as a chemical process, it must be useful to write things up in terms of the extent of reaction ξ, hence $(d_t G)_{T,P,\Phi_j} = \sum_i \mu_i^\dagger d_t N_i$ is rewritten by means of the definition of the so-called stoichiometric coefficient $v_i = \frac{\partial N_i}{\partial \xi}$ and of the chemical affinity $\mathcal{A} = \sum_i \mu_i^\dagger v_i$. The stoichiometric coefficients and the chemical affinities could be defined likewise for a set of $(k = 1 \ldots R)$ regulatory interactions (considered as *chemical reactions*) as follows:

$$d_t G = -\Psi d_t T + \sum_k \mathcal{A}_k d_t\xi_k + \sum_j \mathcal{X}_j \odot d_t\Phi_j \tag{27}$$

or

$$d_t G = -\Psi d_t T + \sum_k \left[\sum_i \mu_{i,k}^{\dagger} \nu_{i,k} \right] d_t \xi_k + \sum_j \mathcal{X}_j \odot d_t \Phi_j. \qquad (28)$$

4.4. Mean field approach

In many cases the explicit stoichiometry of the regulatory interactions is unknown, and in the vast majority of the already studied cases the reactions are given on a one-to-one basis, i.e., one molecule of a transcription factor on each gene transcription site (or one molecule of each kind of transcription factor in the case of multi-regulated gene targets). Given this, at the moment we will assume $\nu_i = 1$; $\forall i$. In this *diluted* case, we find that the extent of each reaction is then proportional to the concentration rate of change and we recover the non-reactive regime similar to that given by Eq. (26). It is important to stress that this approximation is not a disparate one given the fact that the usual DNA/RNA concentrations within the cells are in the picomolar-nanomolar regime. Also, of the almost 30,000 different genes in humans, just a small number of these (about 1000–1500) are known to be transcription factors. Nevertheless, in order to take into account the scarce yet important gene regulatory interactions (albeit in an indirect manner), we retain the generalized force-flux terms to get

$$d_t G = -\Psi d_t T + \sum_i \mu_i d_t C_i + \sum_j \mathcal{X}_j \odot d_t \Phi_j. \qquad (29)$$

Since gene regulation occurs within the cell, it is possible to relate an internal *work* term with the regulation process itself, this being a *far from equilibrium* contribution. This non-local contribution is given by the generalized force-flux term (third term in the r.h.s. of Eq. [29]). This is the case because gene regulation often does not occur *in situ* and also because it is the only way to take into account (albeit indirectly) the changes in the local chemical potentials that cause the long tails in the fluctuations distributions characteristic of non-equilibrium small systems (e.g., cells). The term relating mRNA *flows* due to transcriptional regulation could be written as a product of extended fluxes Φ_j and forces $\mathcal{X}_j$. Here $j = 1, \ldots M$ refers to the different mRNA species being regulated, that is, indexes i and j refer to the very same set of mRNA transcripts but in one case (i) we take into account their local equilibrium behavior (as given by their independent chemical potentials and average local concentrations) and in the other case (j) we are interested in their highly fluctuating (far from equilibrium) behavior as given by the term $\sum_j \mathcal{X}_j \odot d_t \Phi_j$

Now we are faced with the task of proposing a form for the extended fluxes and forces within this highly fluctuating regime, which at the same time allows for experimental verification, is simple enough to be solved, and it is compatible with the axioms of extended irreversible thermodynamics. As a first approach, we are proposing a system of linear (in the forces) coupled fluxes with memory that was used to successfully characterize another highly fluctuating system, a fluid mixture near the critical point [29].

The constitutive equations are

$$\vec{\Phi}_j(\vec{r}, t) = \sum_k \int_{-\infty}^{t} \lambda_{j,k}^{\Phi} \vec{u} \, e^{\frac{(t'-t)}{\tau_j^{\Phi}}} \mu_{j,k}(\vec{r}, t') dt', \tag{30}$$

$$\vec{X}_j(\vec{r}, t) = \int_{-\infty}^{t} \lambda_j^{X} \, e^{\frac{(t''-t)}{\tau_j^{X}}} \vec{\Phi}_j(\vec{r}, t'') dt''. \tag{31}$$

The λ's are time-independent, but possibly anisotropic amplitudes, $\vec{u}$ is a unit vector in the direction of mass flow (the nature of $\vec{u}$ will not affect the rest of our description, since we will be dealing with the magnitude of the mass flux $|\vec{\Phi}_j|$), and τ's are the associated relaxation times considered path-independent scalars. Since we have a linear relation between thermodynamic fluxes and forces, some features of the Onsager–Casimir formalism will still hold. This will be especially important when considering cross-regulatory interactions. An interesting question for future research will be whether gene transcription interactions as modeled here obey Onsager's reciprocal relations.

Dynamic coupling is given by Eqs. (30) and (31); nevertheless, due to the fact that actual transcription measurement experiments are made either on homeostasis (steady state) settings or within time series designs with intervals several orders of magnitude larger than the associated relaxation times (which are of the order of a few molecular collision times), it is possible to take the limits $\tau_j^{\Phi} \to 0$ and $\tau_j^{X} \to 0$, then the integrals become evaluated delta functions, giving:

$$\vec{\Phi}_j(\vec{r}, t) = \vec{u} \sum_k \lambda_{j,k}^{\Phi} \mu_{j,k}(\vec{r}, t), \tag{32}$$

$$\vec{X}_j(\vec{r}, t) = \lambda_j^{X} \vec{\Phi}_j(\vec{r}, t). \tag{33}$$

It is important to note that in the future, it will surely become possible to experimentally measure gene expression in time intervals much shorter (maybe even in real time). In that case, the appropriate theoretical setting will be given by Eqs. (30) and (31), which represent the dynamic nature of the coupling better than Eqs. (32) and (33).

Also due to the spatial nature of the experimental measurements (either RNA blots or DNA/RNA chips measure space-averaged mRNA concentrations), it is possible to work with the related scalar quantities instead, giving

$$\Phi_j(\vec{r}, t) = \sum_k \lambda_{j,k}^\Phi \, \mu_{j,k}(\vec{r}, t), \tag{34}$$

$$X_j(\vec{r}, t) = \lambda_j^X \, \Phi_j(\vec{r}, t). \tag{35}$$

Substituting Eqs. (34) and (35) into Eq. (29), one gets

$$d_t G = -\Psi d_t T + \sum_i \mu_i d_t C_i + \sum_j \sum_k \left(\lambda_{j,k}^\Phi \, \mu_{j,k} \right) d_t \left(\lambda_j^X \, \Phi_j \right). \tag{36}$$

Assuming the generalized transport coefficient λ_j^X to be independent of the flux Φ_j we are able to write

$$d_t G = -\Psi d_t T + \sum_i \mu_i d_t C_i + \sum_j \sum_k \left(\lambda_{j,k}^\Phi \, \mu_{j,k} \right) \lambda_j^X d_t \Phi_j. \tag{37}$$

Or in terms of the transcription regulation *chemical potentials* $\mu_{j,k}$,

$$d_t G = -\Psi d_t T + \sum_i \mu_i d_t C_i$$
$$+ \sum_j \sum_k \left(\lambda_{j,k}^\Phi \, \mu_{j,k} \right) \lambda_j^X \left(\lambda_{j,k}^\Phi d_t \mu_{j,k} + \mu_{j,k} d_t \lambda_{j,k}^\Phi \right). \tag{38}$$

In the constant transport coefficient approximation, Eq. (38) reads

$$d_t G = -\Psi d_t T + \sum_i \mu_i d_t C_i + \sum_j \sum_k (\lambda_{j,k}^\Phi)^2 \lambda_j^X \mu_{j,k} \, d_t \mu_{j,k}. \tag{39}$$

Defining

$$L_{j,k} = \frac{(\lambda_{j,k}^\Phi)^2 \lambda_j^X}{2},$$

we get

$$d_t G = -\Psi d_t T + \sum_i \mu_i d_t C_i + \sum_j \sum_k L_{j,k} \, d_t \mu_{j,k}^2. \tag{40}$$

It is possible to see from Eq. (40) that genetic transcription could be characterized as a *second-order* effect; this arises from the fact that the actual

mechanism of gene expression is regulation by other gene products such as enzymes and transcription factors:

$$d_t G = -\Psi \, d_t T + \sum_i \mu_i d_t C_i + \sum_j \sum_k L_{j,k} \, d_t \mu_{j,k}^2. \tag{41}$$

As we have stated, fluorescence intensity signals as measured by, for example, microarray experiments (i.e., gene chips) are the usual technique used to acquire information about the concentration of a given gene under certain cellular conditions. From Eq. (2), the concentration of a given gene-probe (with hybridization energy ΔG_i) is a function of the intensity as follows:

$$c_i = \frac{\varphi_i}{A_i e^{-\beta \Delta G_i} - \varphi_i e^{-\beta \Delta G_i}}. \tag{42}$$

It is not unreasonable to consider that the local single-species *energy of formation* for a given mRNA transcript (i.e., the partial chemical potential μ_i in Eq. [41]) has the same (absolute) value as the chemical potential of hybridization for the same mRNA species, as given by Eq. (13) such that $\mu_i = +RT/c_i$ could be used in the thermodynamical characterization of gene expression as given by Eq. (41). If we insert Eq. (42) into Eq. (13) we get

$$\mu_i = \frac{RT \left(A_i e^{-\beta \Delta G_i} - \varphi_i e^{-\beta \Delta G_i} \right)}{\varphi_i}. \tag{43}$$

Now, by taking the time derivative of Eq. (42),

$$\frac{dc_i}{dt} = \frac{A_i \, e^{-\beta \Delta G_i}}{\left(A_i \, e^{-\beta \Delta G_i} - \varphi_i \, e^{-\beta \Delta G_i} \right)^2} \left[\frac{d\varphi_i}{dt} \right]. \tag{44}$$

By substitution of Eqs. (43) and (44) into Eq. (41):

$$d_t G = -\Psi \, d_t T + \sum_i \frac{A_i \, e^{-\beta \Delta G_i}}{\beta \varphi_i \left(A_i \, e^{-\beta \Delta G_i} - \varphi_i \, e^{-\beta \Delta G_i} \right)} \, d_t \varphi_i$$
$$+ \sum_j \sum_k L_{j,k} \, d_t \mu_{j,k}^2. \tag{45}$$

If we define

$$\Gamma_i = \frac{A_i \, e^{-\beta \Delta G_i}}{\beta \varphi_i \left(A_i \, e^{-\beta \Delta G_i} - \varphi_i \, e^{-\beta \Delta G_i} \right)}$$

as the *thermodynamic* conjugate variable to the probe intensity φ_i, we obtain

$$d_t G = -\Psi \, d_t T + \sum_i \Gamma_i \, d_t \varphi_i + \sum_j \sum_k L_{j,k} \, d_t \mu_{j,k}^2. \tag{46}$$

5.   Results and discussion

Let us examine in some detail the structure of Eq. (46). In the isothermic, non-regulated steady state (i.e. $d_t G = 0$, $d_t T = 0$, $d_t \mu_{j,k}^2 = 0 \ \forall j, k$), Eq. (46) is nothing but a formal non-equilibrium extension of the Gibbs–Duhem relation $\sum_i \Gamma_i \, d_t \varphi_i = 0$. Without any gene regulatory mechanism, and without explicit dissipation, the energetics of gene expression within a cell are just the ones of a non-interacting dilute mixture of its components (in this case, the different mRNA transcripts). A more realistic case is the regulated, isothermal steady state given by $d_t G = 0$, $d_t T = 0$, and at least some $d_t \mu_{j,k}^2 \neq 0$. This is the more interesting case that one can compare with actual gene transcription experiments nowadays. This is so because, on the one hand, due to the specific nature of nucleic acids (both DNA and RNA suffer thermal decay) and also due to physiological conditions, temperature changes are subtle or negligible within the living cell or inside a realistic biological assay.

The steady-state condition is more of a *present-time situation* than a definitive limitation. Most dynamic gene expression studies nowadays are studied as time series (or *time courses* in the biomedical language) with time steps dictated by economical or pharmacological and not by biophysical reasons. Typically, the smaller time steps are of the order of minutes if not hours or days. Regulatory changes can thus be measured just in their steady-state mean-field contributions (coarse grained in space and time) and not in their whole dynamical complexity. Of course, as the costs of microarray processing lower and as the technologies advance, one expects to see better resolution time series for transcriptional dynamics.

Let us then consider the regulated isothermal steady-state version of Eq. (46), namely:

$$\sum_i \Gamma_i \, d_t \varphi_i + \sum_j \sum_k L_{j,k} \, d_t \mu_{j,k}^2 = 0. \tag{47}$$

One could see that changes in the mRNA concentration of gene i as measured by its probe intensity φ_i could depend *not only on their own* characteristic thermodynamical parameters (A_i, ΔG_i, and T) but also on another mRNA transcript (say n) via a coupling given by a term $L_{n,i} \, \mu_{n,i}^2$. In that case, one says that the n-th gene regulates the i-th gene, or that n is a *transcription factor* for i (conversely, i is a *transcriptional target* of n).

In order to give a concrete example (for the sake of clarity), we will consider the irreversible thermodynamic coupling that sets the process of transcriptional regulation between two genes, *Genes* $= \{1, 2\}$. In this case we will assume that gene number 1 is a transcription factor for gene number 2 and that gene 1 is non-regulated (i.e., gene 1 is not a target for any TF). This means

that $\mu_{1,2} \neq 0$ and that $\mu_{1,1} = \mu_{2,1} = \mu_{2,2} = 0$. In this case, Eq. (47) will read

$$\Gamma_1 \, d_t \varphi_1 + \Gamma_2 \, d_t \varphi_2 + L_{1,2} \, d_t \mu_{1,2}^2 = 0. \tag{48}$$

To make explicit calculations from experimental data we will consider *SYK*, the transcript responsible for the synthesis of *spleen tyrosine kinase* as gene 1 and *IL2RB* or *interleukin 2 receptor, beta* as gene 2. *SYK* is well known for being a strong inducer of gene transcription, especially in the case of the beta domain interleukin 2 receptor [30]. Also, there is strong evidence indicating the possible role of these two genes in the course of the so-called C-MYC network of reactions, a very important, cancer-related biochemical pathway.

The values of the parameters could be calculated as follows. According to the algorithm developed by Lu et al. [6] and described by Carlon et al. (cf. table 1 of reference [5]), it is possible to obtain suitable values for $\Delta G_1 = 483.55$ kcal/mol and $\Delta G_2 = 463.05$ kcal/mol (see Table 1). From these values, we can calculate A_1 and A_2 from Eq. (2) following saturation measurements in the *latin square* experiments [5–7]. In this case $A_1 = 5513$ intensity units/mol and $A_2 = 1105$ intensity units/mol (see Figures 1 and 2).

Given these parameters, from a time-course GEA it is possible to calculate both $\Gamma_1 = \Gamma_1(\varphi_1)$ and $\Gamma_2 = \Gamma_2(\varphi_2)$, and via $\varphi_1(t)$ and $\varphi_2(t)$ we could as well obtain the time evolution for $\mu_{1,2}$, hence characterizing in a complete form the transcriptional regulation for this simple (almost trivial from the biological standpoint) *gene switch*.
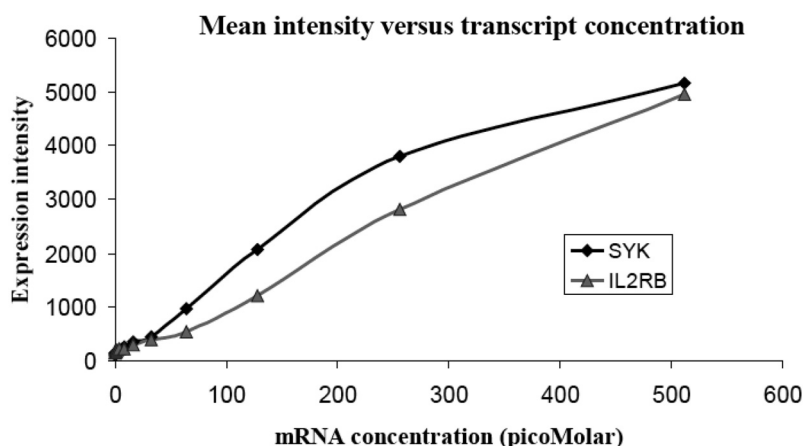
Figure 1   Gene expression intensity as a function of mRNA concentration for *SYK* and *IL2RB*.

Table 1 Thermodynamic data for gene transcripts included in the Latin Square experiments. ΔG_{tr} at 37 °C are calculated according to reference [5].

probeset_key	Gene	Gene name	Transcription factor activity	ΔG_{tr} at 37 °C (Kcal/mol)
203508_at	TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B		502.52
204563_at	SELL	selectin L		446.34
204513_s_at	ELMO1	engulfment and cell motility 1		471.35
204205_at	APOBEC3G	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G	Reverse TF	477.38
204959_at	MNDA	myeloid cell nuclear differentiation antigen	TF regulation	433.97
207655_s_at	BLNK	B-cell linker		436.55
204836_at	GLDC	glycine dehydrogenase (decarboxylating)		468.99
205291_at	IL2RB	interleukin 2 receptor, beta		463.05
209795_at	CD69	CD69 molecule		398.72
207777_s_at	SP140	SP140 nuclear body protein	TF activity	700.57
204912_at	IL10RA	interleukin 10 receptor, alpha		474.56
205569_at	LAMP3	lysosomal-associated membrane protein 3		636.01
207160_at	IL12A	interleukin 12A		453.31
205692_s_at	CD38	CD38 molecule		569.56
212827_at	IGHM	immunoglobulin heavy constant mu		482.07
209606_at	PSCDBP	cytohesin 1 interacting protein		458.19
205267_at	POU2AF1	POU class 2 associating factor 1	TF regulation	473.5
204417_at	GALC	galactosylceramidase		410.95
205398_s_at	SMAD3	SMAD family member 3	TF activity + Binding	465.08
209734_at	NCKAP1L	NCK-associated protein 1-like		716.67
209354_at	TNFRSF14	tumor necrosis factor receptor superfamily, member 14		782.09
206060_s_at	PTPN22	protein tyrosine phosphatase, non-receptor type 22		414.77
205790_at	SKAP1	src kinase associated phosphoprotein 1	TF	452.57
200665_s_at	SPARC	secreted protein, acidic, cysteine-rich (osteonectin)		443.24
207641_at	TNFRSF13B	tumor necrosis factor receptor superfamily, member 13B	TF inducer	481.8
207540_s_at	SYK	spleen tyrosine kinase	TF inducer	483.55
204430_s_at	SLC2A5	solute carrier family 2 (facilitated glucose/fructose transporter), member 5		488.56
203471_s_at	PLEK	pleckstrin		459.23
204951_at	RHOH	ras homolog gene family, member H	TF regulation	467.94
207968_s_at	MEF2C	myocyte enhancer factor 2C	TFact, RNAPol ind	472.81

Intensity amplitude coefficient
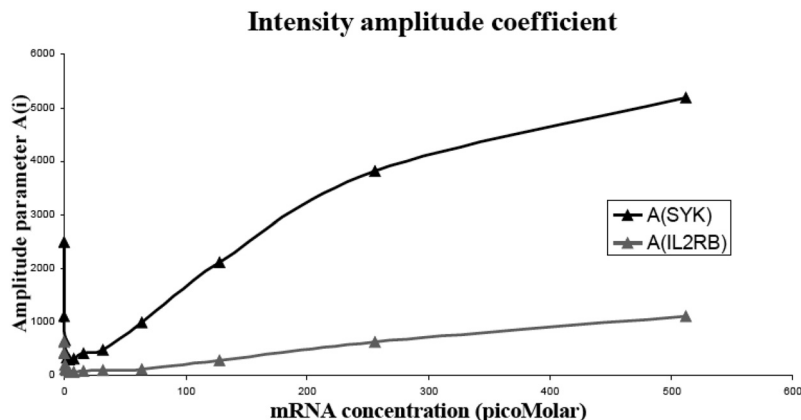
Figure 2 Intensity amplitude coefficient as a function of mRNA concentration for *SYK* and *IL2RB*.

Taking the aforementioned values, we have the following expressions for the thermodynamic functions in terms of the experimentally measurable intensities (in all cases, a physiological temperature of $T = 37\,^{\circ}\mathrm{C}$ is assumed), hence $\beta = 1.622507 \times 10^{-6}$ mol kcal^{-1}, $e^{-\beta \Delta G_1} = 0.99922$, $A_1 \times e^{-\beta \Delta G_1} = 5508.67950$ intensity units/mol; also $e^{-\beta \Delta G_2} = 0.99925$, and $A_2 \times e^{-\beta \Delta G_2} = 1104.17014$ intensity units/mol.

Calculating the intensity-dependent chemical potentials we obtain, from Eq. (43) kcal/mol,

$$\mu_1 = \frac{3.395 \times 10^9 - 6.158 \times 10^5\ \varphi_1}{\varphi_1} \tag{49}$$

and

$$\mu_2 = \frac{6.805 \times 10^8 - 6.159 \times 10^5\ \varphi_2}{\varphi_2}. \tag{50}$$

As we could see from Eqs. (49) and (50) (Figure 3), there is a difference in the transcriptional behavior of gene 1 (*SYK*), which is a transcription factor, and gene 2 (*IL2RB*), which is not (and, in fact, is a transcriptional target). The maximum intensity (related to a maximum concentration peak) attainable in both cases in the spontaneous regime is of 5513 intensity units for *SYK*, whereas in the case of *IL2RB* is of just 1105 intensity units. This means that, in order for *IL2RB* to be produced at higher rates, the presence of chemical environment modifications (e.g., via transcription factors) is needed.
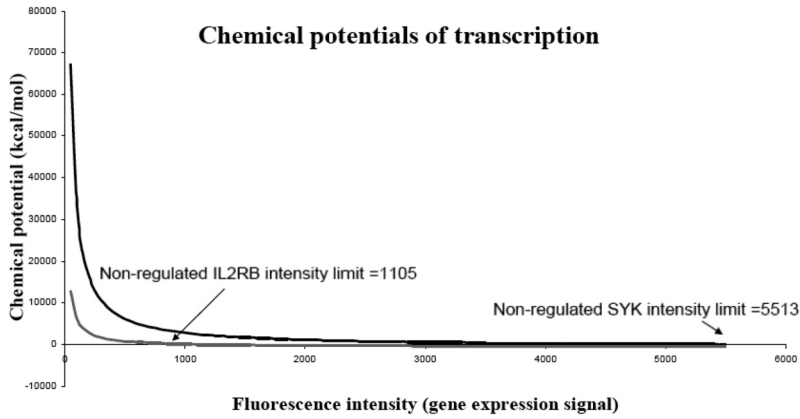
Figure 3 Individual chemical potentials for non-regulated transcription μ_{SYK} and μ_{IL2RB} as a function of gene expression intensity.

In a very straightforward way (similar to our μ_i calculations), we are now able to calculate expressions for Γ_1 and Γ_2 as follows (see Figure 4):

$$\Gamma_1 = \frac{5508.6795}{0.008938 \; \varphi_1 - 1.6098 \times 10^{-6} \; \varphi_1^2} \tag{51}$$

$$\Gamma_2 = \frac{1104.17014}{0.001795 \; \varphi_2 - 1.6243 \times 10^{-6} \; \varphi_2^2}. \tag{52}$$
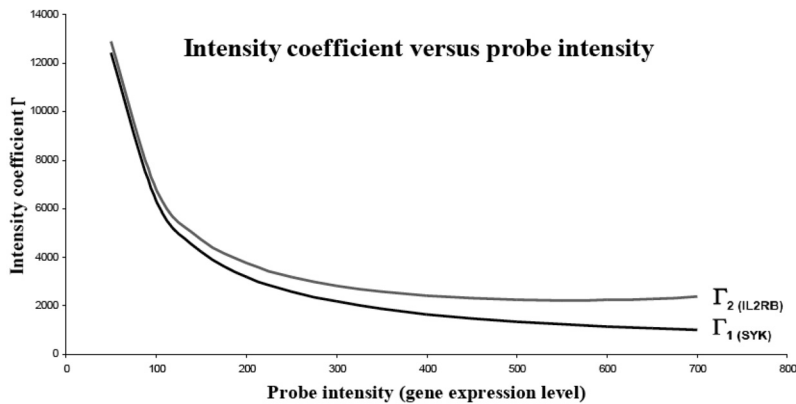
Figure 4 Intensity parameters for non-regulated transcription Γ_{SYK} and Γ_{SYK} as a function of gene expression intensity.

If we substitute Eqs. (51) and (52) into Eq. (48), we obtain

$$-L_{1,2}\, d_t \mu_{1,2}^2 = \frac{5508.6795}{0.008938\ \varphi_1 - 1.6098 \times 10^{-6}\ \varphi_1^2}\, d_t \varphi_1,$$

$$+ \frac{1104.17014}{0.001795\ \varphi_2 - 1.6243 \times 10^{-6}\ \varphi_2^2}\, d_t \varphi_2 \qquad (53)$$

integrating

$$-L_{1,2}\mu_{1,2}^2 = 616321.2687 \ln \left| \frac{-1.6098 \times 10^{-6}\ \varphi_1}{0.008938 - 1.6098 \times 10^{-6}\ \varphi_1} \right|$$

$$+ 615, 136.5683 \ln \left| \frac{-1.6243 \times 10^{-6}\ \varphi_2}{0.001795 - 1.6243 \times 10^{-6}\ \varphi_2} \right|. \qquad (54)$$

Taking experimental values of $\varphi_1(t)$ and $\varphi_2(t)$, Eq. (54) could be solved for $\mu_{1,2}(t)$. As we already stated, both *SYK* and *IL2RB* are involved in the transcriptional network related to the C-MYC pathway, which is very important in the development of cancer.

In order to capture subtle regulatory dynamics, one will need experiments with a large number of smaller time-step measurements, but in principle one is able to observe detailed patterns even within this very simple thermodynamic model.

Interestingly, for this single gene switch it is also possible to calculate the dependency of the transcriptional regulation coupling $\mu_{1,2}$ on the particular cellular environment by solving Eq. (54) for the same two genes under different phenotypical conditions (e.g., cancer versus normal cells, treated vs untreated diseased cells, etc.). The systematic study of such thermodynamic cellular-context transcription regulation theory seems to be a promising research area in the non-equilibrium thermodynamics of biosystems. In conclusion, we have showed here that a non-equilibrium thermodynamical description of cell-level transcriptional regulation could be formulated in terms of experimentally measurable quantities, and that essential features of gene regulatory dynamics could be studied with it. The model has been progressively simplified to match with todays technological and practical limitations; nevertheless these simplifications are not necessary in principle, and can be eliminated when better experimental resolution (specially with regards to more samples and time points) can be attained.

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Book Review

The book gives a very clear presentation about hydrodynamic fluctuations in fluid and fluid mixtures. The nature of these fluctuations around non-equilibrium states is surprisingly different from their equilibrium behaviour. In equilibrium, density and temperature fluctuations are correlated over a distance of the order of the size of the molecules, if one is not close to a critical point or line. Away from equilibrium, new terms appear which have algebraic long ranged tails.

The authors discuss the various misconceptions along the road to the present understanding in a very thorough and entertaining way. In particular the microscopic picture proposed by Bogoliubov (1946, 1962) is incorrect. It was based on the view that the fluid away from equilibrium would proceed to equilibrium in two distinct stages: first a kinetic stage with a time scale of the order of intermolecular collisions, after which local equilibrium is established; second the macroscopic hydrodynamic stage. Implicit in this assumption is that the long range contributions described in this book do not exist.

Local equilibrium is the proper assumption to understand non-fluctuating hydrodynamic behaviour. It is clearly not correct, however, to use local equilibrium for the correlation functions of the temperature and the densities. As the authors explain, one should add fluctuating contributions to the dissipative fluxes and assume that the fluctuation-dissipation theorems remain valid at the local values of the temperature and densities in non-equilibrium states. This simple assumption of local equilibrium for the fluctuating contributions to the dissipative fluxes leads to the long range contributions in the correlation functions of the temperature and the densities, derived and discussed in this book. The first introductory chapter gives a good overview of these matters.

The second chapter introduces non-equilibrium thermodynamics without fluc-
tuations. It prepares the reader to construct equilibrium and non-equilibrium
solutions around which the analysis of the fluctuations is done. As a first step
towards this goal, fluctuations around equilibrium and their short range na-
ture are discussed in the third chapter. In the same chapter two sources of the
long range contributions in non-equilibrium states are identified. The first is
that the strength of the noise contributions depends for instance on the tem-
perature, which varies through the system. The second are mode-coupling
contributions.

In the fourth chapter, fluctuations are studied for a one-component system in
a temperature gradient, referred to as the Rayleigh-Bénard problem. Bound-
ary effects are ignored. As everywhere in the book the governing equations
are systematically linearized in the fluctuating contributions. Appropriate ap-
proximations are made and the structure factor calculated. It is found that the
resulting Brillouin peaks have different heights. In the equal time correlation
function a long-range contribution proportional to the square of the temper-
ature gradient appears. In the direction normal to the temperature gradient
this contribution is proportional to the inverse of the fourth power of the wave
vector. Similar behaviour is found in the fifth chapter for mixtures.

Chapters six and seven discuss confinement effects. For free boundaries this
is reasonably straightforward. For the more realistic rigid boundaries this
requires considerably more, partly numerical, work. An important result is
that the behaviour of the long range contribution is proportional to the square
of the component of the wave vector normal to the temperature gradient up
to a magnetude comparable to the inverse thickness of the fluid layer, above
which it becomes proportional to the inverse of the fourth power of the wave
vector. An analysis of the real space behaviour is given which shows the long
range nature of these contributions and their dependence on the thickness of
the fluid layer.

Chapter eight treats the behaviour of the fluctuations when one approaches the
Rayleigh-Bénard instability. The authors compare their exact solution with the
results of the most unstable mode approximation and the Swift-Hohenberg
model and conclude that the most unstable mode approximation is much
better.

The analysis in the fifth chapter is extended in the ninth chapter for binary
mixtures to include the effects due to confinement. The tenth chapter dis-
cusses experimental results. In particular light scattering and shadowgraphy
are treated in detail clarifying the experimental consequences of the theoreti-
cal results. This is a very appropriate and useful chapter. In a final chapter the
authors consider a number of problems which are also very interesting: one-

component fluids under shear; a liquid-vapour interface with a temperature gradient along the surface; nematic liquid crystals and a reaction diffusion system. This is material enough to write another book about.

The book is an impressive contribution to the understanding of fluctuations in non-equilibrium systems. The authors are unbelievably thorough. The equations are explained in detail. Solutions are given. Where needed numerical solutions are presented. Approximate solutions are compared with the numerical solutions. The available literature is discussed and results compared. The experimental verification of the results is discussed in some detail. It is a great book.

Dick Bedeaux
Dept. of Chemistry
Norwegian University of Science and Technology
NO-7491 Trondheim, Norway
e-mail: dick.bedeaux@chem.ntnu.no

Book Review*

For textbooks dealing with the fundamentals or with general aspects of a given discipline, it is often difficult to get a clear idea of the viewpoint, level or even contents, when only the title of the work is known. For this reason, when a new book on nonequilibrium thermodynamics appears, one may ask two questions, either openly or tacitly: First: what does the new book contribute to the subject?; and second: how dows it fit into the general landscape already configured by previous monographies?. Regarding the book we review here, one may compare with two previous monographies (although possibly not only those); one is the classical text by Sybren de Groot and Peter Mazur (Nonequilibrium thermodynamics, North-Holland 1962) and the other the work by the same authors: Jou, Casas-Vázquez and Lebon (Extended Irreversible Thermodynamics, Springer 2001). On the one hand, those who learned nonequilibrium thermodynamics from the book by de Groot and Mazur will find in the present book a depth, rigorous, but at the same time swift, exposition of developments not covered by the classical text; including finite-time thermodynamics, instabilities and pattern formation, or fluctuations. In addition, the current book also covers several "modern" theories (sometimes competing, sometimes complementary) that go beyond the local-equilibrium hypothesis; including extended irreversible thermodynamics, rational thermodynamics, theories with internal degrees of freedom (mesoscopic nonequilibrium thermodynamics), and Hamiltonian formalisms (GENERIC). On the other hand, those who know the book "Extended Irreversible Thermodynamics" by the same authors will notice that the aim of the present book is quite different, since it presents on equal foot the various modern theories beyond the local-equilibrium hypothesis. Therefore, the current text should not be considered as an "apology" of extended irreversible thermodynamics. Indeed, in spite of

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*The contents of this book review are partly based on a comment previously published (in Spanish) in the *Revista Iberoamericana de Física*.

being considered the fathers of this particular "extension" of nonequilibrium thermodynamics, the authors make here a successful effort to present the work of all modern schools evenly; letting the theories speak for themselves and looking for points of contact, so as to present them as more complementary than one might initially expect.

The book is intended for a graduate-level course on the subject. In little more than 300 pages we meet a pedagogically neat presentation of the material, where topics (historical notes or detailed deductions of some equations) that may distract the attention of the reader, are inserted into "boxes". Furthermore, at the end of each chapter, a set of problems is proposed. Unfortunately, solutions to these exercises are not presented; omission that would not please many readers, especially since some of these problems have a quite high level of difficulty.

In the preface it is indicated that the book can be divided into two parts, the first part (chapters 1–6) is essentially an introductory course to equilibrium and nonequilibrium thermodynamics, the second part covers topics that are more "specialized". It turns out that all the material presented in chapters 1–6 is based on the local-equilibrium hypothesis, while in chapter 7 and subsequent chapters this assumption is abandoned, covering topics beyond the classical theory. Indeed, the second part contains basic introductions and comparison of the various approaches going beyond local equilibrium (extended irreversible thermodynamics, rational thermodynamics, internal variables, Hamiltonian formalisms). The result is quite interesting for a graduate-level course, since the content of this second part gradually and smoothly places the students on the research frontier. As already mentioned, the authors try hard to treat all ideas on an equal footing, establishing equivalences and making points of contact, to almost show all of them as complementary. They try not to prioritise any school over the others, and conclude at the Epilogue by saying that is the reader who has to make up his personal opinion.

However, one of the criticisms that could be raised to the general structure of the current book is the delay of the study of fluctuations to the last chapter 11. From a conceptual point of view, classical nonequilibrium thermodynamics naturally includes a theory of fluctuations based on the local-equilibrium hypothesis. The fluctuation-dissipation theorem and the formulation of Langevin or Fokker-Planck equations for fluctuating thermo-hydrodynamics could be considered as generic tools of classical nonequilibrium thermodynamics and be placed earlier, maybe just before the chapter on instabilities and pattern formation.

Anybody who has ever written a book knows how difficult it is to decide on which topics to include and which ones not to include. This challenge of

selecting and optimising contents is a difficult task and full responsibility of the authors. In the current book they made an effort to avoid cumbersome details and try to focus the attention of the reader on the main physical ideas. It may happen that the consequent subject clipping will not please everybody, and even disappoint someone expectations. For instance, in chapter 5, some people would miss a more thoughtful discussion of topics such as global warming, econophysics or ecology. In spite of this, we generally see a very good balance between depth and concision.

The current work, in agreement with the stated textbook philosophy, starts in chapter 1 with a short review of equilibrium thermodynamics, that reflects the many years teaching experience of the authors. The result is very satisfactory, although a more formal presentation of the laws may be missed, and the importance of the equation of state could have been emphasized more strongly. Then, the book goes on in chapters 2–3 studying irreversible processes in the classical framework. The text of these sections is swift and easy to follow. Maybe a more clear distinction between local and material derivatives (page 41) is missing, while the critic of the classical model (pages 63–65) is brilliant. As is well-known, chemical reactions and the link with chemical kinetics may be called the "failed course" of classical nonequilibrium thermodynamics. For this reason it is quite difficult to write meaningfully about this topic. Nevertheless, in chapter 4 the authors are able to negotiate the chemical reaction by including such topics as coupling among reactions, molecular motors and, even, morphogenesis (Turing instabilities); maybe this latter topic would be better placed in the pattern formation chapter though.

It is precisely chapter 6 devoted to instabilities and pattern formation one of the most interesting features of the current textbook. This subject naturally fits in a course of nonequilibrium thermodynamics, and the existence of instabilities is one of the most striking differences between equilibrium and nonequilibrium systems. Some readers would prefer a more detailed discussion of the various topics (in line with the contents of "box 6.1" in page 147), however we believe that the balance reached between clarity and concision in this chapter is quite good. Chapter 6 includes such important topics as Rayleigh-Bénard, Bénard-Marangoni or Taylor instabilities, as well as Lotka-Volterra or Brusselator models.

Regarding the topics covered in chapters 7–10, in addition to what has been said above, it is worth noticing that a detailed coverage and understanding of this material would require more specialized monographies. It is precisely for this reason that the concision and rigor achieved by the authors in these chapters is very welcome, while presenting at the same time appropriate references for those who want to know more.

In summary, the book reviewed here may be a very useful tool for those whishing to learn nonequilibrium thermodynamics, from the very basics to the research frontier, with a very good balance between depth and broad coverage. It may also be of invaluable help for those teaching or taking graduate-level courses on the subject. It may become a reference work

M. Criado-Sancho
UNED Madrid
Spain
e-mail: ●●●

José M. Ortiz de Zárate
Universidad Complutense
Madrid
Spain
e-mail: ●●●

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