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Article

## Fokker-Planck Equation and Thermodynamic System Analysis

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**Abstract:** The non-linear Fokker-Planck equation or Kolmogorov forward equation is currently successfully applied for deep analysis of irreversibility and it gives an excellent approximation near the free energy minimum, just as Boltzmann's definition of entropy follows from finding the maximum entropy state. A connection to Fokker-Planck dynamics and the free energy functional is presented and discussed—this approach has been particularly successful to deal with metastability. We focus our attention on investigating and discussing the fundamental role of dissipation analysis in metastable systems. The major novelty of our approach is that the obtained results enable us to reveal an appealing, and previously unexplored relationship between Fokker-Planck equation and the associated free energy functional. Namely, we point out that the dynamics may be regarded as a gradient flux, or a steepest descent, for the free energy.

**Keywords:** entropy generation; Fokker-Planck equation; irreversible systems; non-equilibrium thermodynamics

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## 1. Introduction

Stochastic differential equations are used to model many complex systems in physics, chemistry, biology, economics, and engineering, including population dynamics, protein kinetics, turbulence, *etc.* In this context, the Fokker-Planck equation represents the probability density for the position or the velocity of a particle which motion is well described by Langevin's equation and how a collection of their initial physical data evolves with time. The Fokker-Planck equation is an excellent approximation near free energy minima. The solution of the Fokker-Planck equation is a powerful tool that allows one to follow at each instant the direction of a gradient flux of the associated free energy functional by a discrete time formulation, based on the Wasserstein metric [1]. By this approach metastability and hysteresis in physical systems could be treated in a satisfactory way [1–4]. Moreover, these results underline also the role of the dissipation analysis in metastable systems: a connection exists between Fokker-Planck equation and the global thermodynamic quantities like entropy, needed in the analysis of the dissipation in irreversible systems. As underlined in many papers (see for instance [5,6] and references therein quoted), entropy production and entropy generation are different concepts. The main characteristics of entropy generation [7–13] are: (a) it introduces the lifetime of the process, *i.e.*, the time of occurrence of a process and (b) it allows the analysis of the systems in a time greater than or equal to the lifetime of the entire process, while the entropy production needs the local equilibrium hypothesis and it does not consider the time at all. Moreover, entropy generation is a global effect, while entropy production is its local counterpart; indeed entropy production is the entropy generation density rate. These two quantities are different: the local form usually does not allow the description of the cooperative effect of the irreversibility, as it has been shown in the optimization studies of thermal engineering [6,7]. Entropy production and entropy generation are two possible approaches to the analysis of irreversibility, in the present work entropy generation has been used due to the link with thermal engineering applications. For system dissipation analysis the two approaches are complementary. In this paper we apply Fokker-Planck equation to dissipation phenomena, with particular regards to the entropy generation and we come to a consistent statistical description.

## 2. The Non-equilibrium Fokker-Planck Equation

According to what has been said in the previous paragraph, Fokker-Planck equation is considered for a set of  $n$  interacting particles. Each particle position evolves in time following Langevin's equations:

$$\frac{dx_i}{dt} = f_i(\mathbf{x}) + r_i(t) \quad (1)$$

where  $x_i$  is the position of the  $i$ -th particle,  $\mathbf{x} = \{x_i\}$ ,  $f_i$  is the force acting on the  $i$ -th particle,  $r_i$  is the noise-induced drift term due to diffusion gradient effects (if the noise is state dependent). The noise term  $r_i$  is a stochastic variable that obeys a Gaussian probability distribution with correlation function such as:

$$\begin{aligned} \langle r_i(t) \rangle &= 0 \\ \langle r_i(t)r_j(t') \rangle &= 2D_i\delta_{ij}\delta(t-t') \end{aligned} \quad (2)$$

with  $D_i \geq 0$  is a different constants for each particle. This implies the Onsager reciprocity relation  $\delta_{ij} = \delta_{ji}$  for the dumping coefficients. The  $\delta$ -function of the correlations in time means that  $r_i(t)$  at a timer  $t$  is assumed to be completely uncorrelated with it a any other time.

In order to compute physical quantities we have to perform averages with respect to the noise: this is the consequence of the use of the entropy generation. The small perturbations of the systems can be neglected because times much longer with respect to the perturbations themselves have been considered, and then we take for physical quantities only time averages. In this approach, noise is described as a term of the entropy generation and it could be explicitly written as a sum of effects when specific applications are considered.

Then the Fokker-Planck equation describing the time evolution of the probability distribution  $P(\mathbf{x},t)$ , usually named Smoluchowski equation, can be written as [8,14]:

$$\frac{\partial P(\mathbf{x},t)}{\partial t} = -\sum_i \frac{\partial J_i(\mathbf{x},t)}{\partial x_i}$$

$$J_i(\mathbf{x},t) = \left[ f_i(\mathbf{x}) + D_i \frac{\partial}{\partial x_i} \right] P(\mathbf{x},t) \tag{3}$$

Equation (3) can be solved inside a space spanned by the variable set  $\mathbf{x} = \{x_i\}$ , under boundary conditions related to the behavior of  $P(\mathbf{x},t)$  and  $J_i(\mathbf{x},t)$  at the boundary surface of the integration space itself. The condition of irreversibility can be expressed as follows:

$$D_i \neq D_j \quad i \neq j \quad \text{or}$$

$$D_i = D_j = D \quad i \neq j \quad \text{but} \quad \frac{\partial f_i}{\partial x_j} \neq \frac{\partial f_j}{\partial x_i} \tag{4}$$

The first part of (4) can represent a system in contact with two or more heat reservoirs at different temperature, while the second relation can describe the contact of an irreversible system with one heat reservoir, but in the case of non-conservative forces. Equations (4) finds a useful application if we consider a thermodynamic approach to molecular machine. In fact, a thermodynamic machine works between two heat reservoirs and this case will be analyzed as a case example in one of the following sections. Generally speaking a thermodynamic system is a physical system whose interactions with the environment are characterized by transfer of heat and work. For such system, it is possible to write the kinetic energy theorem as [15,16]:

$$W_{es} + W_{fe} + W_i = \Delta E_k \tag{5}$$

where  $W_{es}$  is the work done by the environment (the world outside the system) on the system, in other words the work done from external forces on the border of the system,  $W_{fe}$  is the work lost due to external irreversibility (outside energy dissipation),  $\Delta E_k$  is the kinetic energy of the system,  $W_i$  is the internal work, such that:

$$W_i = W_i^{rev} - W_{fi} \tag{6}$$

with  $W_i^{rev}$  the reversible internal work and  $W_{fi}$  the work lost due to internal irreversibility. Moreover, the following relation must be taken in account [15,16]:

$$W_{se} = -W_{es} - W_{fe} \quad (7)$$

where  $W_{se}$  is the work done by the system on the environment, *i.e.*, the work done from internal forces on the border of the system. It is then possible to obtain the following two equivalent equations from the First Law of Thermodynamics:

$$Q - W_{se} = \Delta U + \Delta E_k \quad (8)$$

$$Q - W_i = \Delta U \quad (9)$$

being  $U$  the internal energy of the system. Now, by using the relations (5), (6) and (9), it follows that:

$$W_{fi} = Q - W_i^{rev} - \Delta U \quad (10)$$

and from (7) and (9), Equation (10) becomes:

$$W_{fi} = -W_{fe} - W_i^{rev} - W_{es} + \Delta E_k \quad (11)$$

In a stationary state the kinetic energy, the work done external to the systems and the internal reversible work are all constant, therefore:

$$\delta W_{fe} = -\delta W_{fi} \quad (12)$$

applying Gouy-Stodola theorem that states:

$$W_{fe} = T_0 S_g \quad (13)$$

it follows that:

$$\delta W_{fe} = -T_0 \delta S_g \text{ from outside of the system} \quad (14)$$

$$\delta W_{fe} = T_0 \delta S_g \text{ from inside of the system} \quad (15)$$

The possible extrema are opposite, maximum if evaluated from the outside and minimum from the inside. The Equations (14) and (15) show the total work lost due to external irreversibility  $W_\lambda$ . These results underline the connection between the entropy generation and the work (energy) inside the system balanced on the boundary between the system and the environment and even provide a new approach to highlight the interaction between the system and its environment. Indeed, we are highlighting that irreversibility is the core of the whole entropy generation approach. The existence of irreversibility is due to the work lost, and this could be considered as a “natural” way of communication between the complex system and its environment. One important aspect is that, being the complex system accessible just due to the irreversible processes, the energy lost towards the environment can be seen as the information lost from the system, but this information is gained by the environment. Complex systems are all the time in a non-equilibrium situation with a continuous energy transduction: cell molecular machines are typical examples. A cell molecular machine can transport matter along the cell as done by kinesin protein in eukaryotic cells, or can propel the cell through the extracellular media, as the case of bacterial flagellar motor. In both cases they use energy from electrochemical potential variations or from the hydrolysis of the ATP. The ATP diffusion process inside the cell is a diffusion process and it can be worthy studied by Fokker-Planck equation and entropy generation approach as we show in the next paragraph.

### 3. Entropy Generation and Fokker-Planck Equation

Since 1962, Jaynes argued that Gibbs’ formalism of equilibrium statistical mechanics could be generalised in a statistical inference theory for non-equilibrium systems [17]. Moreover, the fluctuation theory has been established for a variety of non-equilibrium systems. In [17] it is said that probability of violation of the Second Law of thermodynamics becomes exponentially small as  $\tau$  (or the system size) increases, with  $\tau$  the time duration of the physical process. Therefore, it has been developed non-equilibrium statistical mechanics for the stationary state constraint on the basis of maximum entropy [17]. The approach consists of maximising the path of Shannon’s information entropy written as  $S_I = -\sum_\gamma p_\gamma \ln p_\gamma$ , with respect to  $p_\gamma$  on the path  $\gamma$ . The information entropy is then seen as the logarithm of the number of the outcomes  $i$  with non-negligible probability  $p_i$ , while in non-equilibrium statistical mechanics approach information entropy is the logarithm of the number of microscopic phase-space paths  $\gamma$  having non-negligible probability  $p_\gamma$ . Following the suggestions of [17] we have to evaluate the most probable macroscopic path realised by the greater number of microscopic paths compatible with the imposed constrained, in full analogy with the Boltzmann microstate counting that claims paths, rather than states, are the central objects of interest in non-equilibrium systems. This because of the presence of non-zero macroscopic fluxes whose statistical description requires to take into account the microscopic behaviour over time. The last statement implies that the macroscopic behaviour is reproducible under known constraints and it is characteristic of each of the great number of microscopic paths compatible with those constraints [17]. From these considerations, it has been proven that the information entropy for the open systems is related to their entropy generation as [18]:

$$S_g = k_B S_I = -k_B \int P_\gamma(\mathbf{x}, t) \ln P_\gamma(\mathbf{x}, t) d\mathbf{x} \tag{16}$$

with  $p_\gamma = P_\gamma(\mathbf{x}, t)$ . One possible interpretation of (16) is the missing information necessary for predicting which path a system of the ensemble takes during the transition from one state to another. Now, considering Gouy-Stodola theorem [7] the entropy generation can be related to the power lost  $\dot{W}_\lambda$  due to irreversibility as expressed in the relations (14) and (15), and it follows:

$$S_g = \frac{1}{T_0} \int_0^\tau \dot{W}_\lambda dt \tag{17}$$

with  $T_0$  reference temperature (usually environmental temperature is taken), thought as a constant. Now the power lost for irreversibility must be obtained. Starting from the definition [8,14]:

$$\dot{W}_\lambda = \left\langle \sum_i f_i \frac{dx_i}{dt} \right\rangle \tag{18}$$

from the Langevin’s Equation (1), the power lost for irreversibility can be written as:

$$\dot{W}_\lambda = \left\langle \sum_i f_i [f_i(\mathbf{x}) + r_i(t)] \right\rangle = \left\langle \sum_i (f_i^2 + D_i f_{ii}) \right\rangle \tag{19}$$

with  $f_{ii} = \partial f_i / \partial x_i$ . Using this relation the entropy generation results:

$$S_g = \frac{1}{T_0} \int_0^\tau \left\langle \sum_i (f_i^2 + D_i f_{ii}) \right\rangle dt = \frac{\tau}{T_0} \left\langle \sum_i (f_i^2 + D_i f_{ii}) \right\rangle \quad (20)$$

This quantity is very interesting because allows us to introduce a reference state ( $T_0$ ) and the characteristic time ( $\tau$ ) of the process considered.

Evaluating the average in the right side of Equation (20) and passing in the continuous setting of the phase-space it can be written:

$$S_g = \frac{\tau}{T_0} \int \sum_i (f_i^2 + D_i f_{ii}) P_\gamma(\mathbf{x}, t) d\mathbf{x} \quad (21)$$

where  $\mathbf{x}$  represent all the possible microscopic phase-space paths and  $P_\gamma(\mathbf{x}, t)$  the associated probability.

The interest of the obtained result can be highlighted in connection to biophysical analysis of cells. This approach can represent a new point of view: instead of studying the cell, that is a very complex system indeed, we think it is easier and worthy to study how cells exchange matters and energy, *i.e.*, information, with their environments, to come up to highlight cell interactions with the environment. Diseases or malfunctions could be seen through pathological cell-environment interactions. Cell-environment interactions are no more than flows across the cell membranes. But cells are so complex that it is almost impossible to quantify the single effect of each cellular process in relation to the global result. Therefore we start to consider the spontaneous flows through cell membranes. The spontaneous heat cell exchange represents the interaction or the spontaneous communication between the cell and its environment. Generally, it is easier to access to the environment than having a look inside the living cell. The heat flow throughout the cell membrane is strictly related to the irreversible processes within cells and this can be easily modelled by Gouy-Stodola theorem. In this way it must be taken into account only the work lost for irreversibility and the temperature of the environment. The obtained results sum up information from global thermodynamic approach and statistical mechanical interpretation of the system.

#### 4. Application to Biological Molecular Machines

In biophysics there is a growing interest in molecular motor analysis (see for instance [19]). The dynamics of such motors are quite different in relation to macroscopic motors. Typical distances, velocities and viscosities of the cellular media overwhelm the dynamics of the motion of the motor; therefore, the inertia doesn't play any role in the physical mathematical approach, while the thermal fluctuations must be considered. The basic dynamics can be well described by the Langevin's Equation (1). For a rotatory motor, it follows that the Equation (1) becomes:

$$x = \vartheta$$

$$f(\mathbf{x}) = \frac{1}{\gamma} (\tau_{in}(\vartheta) + \tau_{ext}) \quad (22)$$

where  $\gamma$  is the effective rotational friction coefficient of the motor,  $\tau_{in}(\vartheta)$  is the internal torque profile generated by chemical processes,  $\tau_{ext}$  is the conservative external torque applied on the motor and  $r(t)$  is the thermal noise described, for instance, as a Gaussian white noise of zero mean value. This approach can be used for a linear motor such as kinesin protein behaviour in eukaryotic cells. In kinesin the linear length of the step is fixed by the periodicity of the dimers of the microtubule track, while for rotatory

motors the angular step depends on the radial symmetry of the motor. Moreover, two different energetic states must be considered:

- (1) the relaxed state, in which the motor does not advance and waits for an energetic input;
- (2) the excited state, in which the energy is transduced producing the power stroke of the motor.

In some biological machines the energy can be obtained by the hydrolysis of the ATP. So, from (3) and (23) it follows that:

$$\frac{\partial P(\vartheta, t)}{\partial t} = -\frac{\partial}{\partial \vartheta} \left[ \frac{1}{\gamma} (\tau_{in}(\vartheta) + \tau_{ext}) + D \frac{\partial}{\partial \vartheta} \right] P(\vartheta, t) \quad (23)$$

with  $D$  a noise function. From (21) and (23) the work lost for irreversibility  $W_\lambda$  can be written as:

$$W_\lambda = T_0 S_g = \tau \int \left[ \frac{1}{\gamma^2} (\tau_{in}(\vartheta) + \tau_{ext})^2 + \frac{1}{\gamma} (\tau_{in}(\vartheta) + \tau_{ext}) D \frac{\partial}{\partial \vartheta} \right] P(\vartheta, t) d\vartheta \quad (24)$$

from (24) we can find out a relation that makes possible to evaluate the efficiency  $\eta$  of the molecular machine:

$$\eta = 1 - \frac{W_\lambda}{\Delta G_{ATP}} = 1 - \frac{\tau}{\Delta G_{ATP}} \int \left[ \frac{1}{\gamma^2} (\tau_{in}(\vartheta) + \tau_{ext})^2 + \frac{1}{\gamma} (\tau_{in}(\vartheta) + \tau_{ext}) D \frac{\partial}{\partial \vartheta} \right] P(\vartheta, t) d\vartheta \quad (25)$$

where  $\Delta G_{ATP}$  is the free energy variation (free energy =  $\Delta G_{ATP} - W_\lambda$ ,  $W_\lambda$  is the work lost for irreversibility and is a constant since a specific process is considered) due to the hydrolysis of a single ATP molecule ( $\sim 21 k_B T = 50 \text{ kJ mol}^{-1}$ , being  $k_B$  the Boltzmann constant and  $T$  the temperature). The Equation (25) shows the connection to efficiency  $\eta$  of the molecular machine and the probability distribution. We can argue that this probability distribution, is strongly related to molecular machines operations and would be different from normal and ill cell, being different the behaviour of the cells and their interactions with the environment. This equation allows us to link the macroscopic power of the molecular machine with the microscopic chemical reaction probability.

## 5. Conclusions

In this paper a Fokker-Planck equation for the entropy generation has been introduced. The result is a thermodynamic approach to irreversibility which links the global analysis to the statistical one. The obtained results show the important role of the entropy generation in analysis and understanding of irreversibility. Our conclusions follow what is pointed out in [11]: it is the energy flow between the system and its environment that renders the evolution irreversible. These flows of energy “select and shape” the paths “delivering least time energy dispersal” [11]. According to [15,16], cells’ behavior could be seen as the consequence of the interplay and dynamic balance between pairs of opposite elements, that are in the present approach the cell system and its environment. In [23–26] it has been pointed out that the two principles, maximum of entropy generation and least action, can be seen as the same fundamental laws of nature. The natural behavior of the open systems could be thought as the decrease of free energy in the least time (minimum). The least time can be evaluated by the entropy generation theorem. Using the entropy generation is possible to analyze the irreversibility in real systems overcoming most of the difficulties rising with the entropy production approach as pointed out by [23,24]. The link between the entropy generation and the Fokker-Planck equation leads to a statistical

approach to the exergy (the maximum useful work possible during the process) flows evaluation. The entropy generation in irreversible processes could represent the basis of a new approach to modern thermodynamics and statistical physics.

### Author Contributions

Both authors contributed at their best at the realization of this paper. The basic idea, namely to approach irreversible systems and non-equilibrium thermodynamics throughout Gouy-Stodola theorem and entropy generation has been developed during the years by Umberto Lucia that has published his previous research results and applications mainly in *Physica A*. Gianpiero Gervino contributed to the statistical physics concepts and suggested the applications in the biophysics contest to study from a new point of view biological molecular machines. Umberto Lucia mainly contributed to second section, Gianpiero Gervino mainly to fourth section, while the third section has been realized with equal contribution of both authors. Both co-authors have been included in the author list and they both have read and approved the final version of the manuscript.

### Conflicts of Interest

The authors declare no conflict of interest.

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