Time-dependent Nonequilibrium Thermodynamics: 
A Master-equation Approach

Hao G.
School of Mathematical Sciences and Center for Computational Systems Biology, Fudan University, Shanghai 200433, P.R. China
(Dated: April 15, 2009)

Master equation could be applied to model various kinds of biochemical systems. A general theory for its time-dependent nonequilibrium thermodynamics is rigorously derived. We not only introduce a concept of general internal energy, but also propose an extension of the equilibrium state. Moreover, we find out an explicit expression for the extended form of the Second Law, which is phenomenologically stated as “the conversion of work to excess heat is irreversible”. The theory is carefully applied to several thermodynamic processes, and its consistence with the classical thermodynamics is clearly shown.

PACS numbers: 05.70.Ln, 82.60.Qr, 02.50.Ga, 05.10.Gg

I. INTRODUCTION

Equilibrium thermodynamics emerges when Carnot proposed the first theoretical treatise on mechanical work and efficiency in heat engines in the early nineteenth century. However, one hundred fifty years after its formulation, the second law of thermodynamics still appears more as a program than a well defined theory, and all the thermodynamic potentials could be well-defined only in equilibrium states. This is one of the main reasons why the equilibrium thermodynamics could hardly be applied to real biochemical systems, because living cells must continually extract energy from their surroundings in order to sustain the characteristic features of life such as growth, cell division, intercellular communication, movement and responsiveness to their environment.

The researches on irreversible systems far from equilibrium began with the works by Prigogine, I. and his collaborators provided explicit expressions for entropy production in various situations, and regarded a nonequilibrium steady state as a stationary open system with positive entropy production rate [4].

In 1998, Oono and Paniconi [5] proposed a framework of steady state thermodynamics, and distinguished the steadily generated heat which is generated even when the system remains in a single steady state and the total heat. They called the former the “housekeeping heat”, which is equal to the entropy production in steady state and may come from the chemical driven force in biochemical systems [6, 7]. The key point of their work is that “if we can carefully remove the steadily produced heat due to housekeeping dissipation, then the state should not be very different from equilibrium”. Moreover, they also put forward a phenomenological extended form of the Second Law: “A process converting work into excess heat is irreversible. And ‘reversibility’ is modulo house-keeping heat, which is produced anyway”.

On the other hand, it has been known for several decades that one can use stochastic processes as mathematical tools to study nonequilibrium states and steady cycle fluxes. In 1953, Onsager and Machlup [8, 9] proposed the Onsager-Machlup principle, which is actually a functional formula about the probability density of a stochastic process close to equilibrium. T.L. Hill [10, 11, 12, 13] and J. Schnakenberg [14] successfully constructed a general mesoscopic master-equation model for biochemical systems and investigated its thermodynamic properties far from equilibrium. Since then, a rather complete mathematical theory for nonequilibrium steady states has been developed for stochastic models [15].

In recent years, a few interesting relations that describe the statistical dynamics of driven systems even far from equilibrium have been discovered, including the fluctuation theorems of sample entropy production [16, 17, 18, 19, 20, 21, 22, 23, 24]. Further, the dissipative work subtracting the excess heat along the trajectory does not depend on the particular “path” taking through the parameter space, namely, only depends upon the initial and final states. Thus, there exactly exists a “general internal energy”, whose derivative is just the difference of the dissipative work and excess heat.

Regarding the Second Law of Thermodynamics, it is shown that the formulation here not only accords
well to its former form, namely the nonnegativity of entropy production, but also put forward another explicit mathematical interpretation for its extended form, which is phenomenologically stated as "the conversion of work to excess heat is irreversible" [5, 23]. The extended form says that the entropy production rate after subtracting the house-keeping heat is still nonnegative, namely \( T \cdot e \sigma(t) - Q_{hk}(t) \geq 0 \), which consequently gives rise to the extended forms of the Clausius inequality and Helmholtz/Gibbs free energy inequalities, and takes Hatano-Sasa’s work as a special example.

Similar result has been put forward in Langevin systems [27], but the analysis here is much more comprehensive.

II. THEORY

Now stochastic models are widely used in physics, chemistry, biology and even in economics. The master-equation process discussed in this article could be applied to model chemical reactions, which are of special interest in biology, in relation with their coupling with active transport across membrane [12, 28] and also recent mechanisms of molecular motors [29]. Furthermore, in real biochemical systems, the external parameters such as the concentrations of external signal proteins always oscillate or remarkably fluctuates, which stimulates the necessity for the analysis of time-dependent processes.

In physics, master equation is a set of first-order differential equations of the mesoscopic system:

\[
\frac{d}{dt} p_i(t) = \sum_{j=1}^{N} \left(q_{ij}(t) p_j(t) - q_{ji} p_i(t)\right),
\]

(1)

describing the dynamical evolution of a probability distribution \( p_i(t) \) over states \( i = 1, 2, \ldots, N \). The quantity \( q_{ij}(t) \) is the transition density (probability per time) to state \( j \) from state \( i \). It contains internal rate constants as well as external conditions imposed by the coupling to the reservoir systems. The basic properties of this model has been discussed previously [30].

One could take a stationary Markov chain, in which the probability transition density \( Q(t) \) is invariant, as the mathematical model of the combination and transformation of biochemical polymers [11, 12]. Each state of the Markov chain corresponds to a mesoscopic state of polymers.

Let us also mention that the number \( N \) need not to be finite, and the system could also be regarded as the stochastic model of coupled chemical reactions (chemical master equation) [14, 51, 52].

A. Essential Notations and Fundamental Relations

Equilibrium thermodynamics is a generalization of mechanics by introducing three new concepts: equilibrium states, internal energy and entropy which related to disorder.

The concept of states is an ensemble of well-defined variables for identifying any property of the system under study. Nowadays, whether the most important quantities in thermodynamics, such as temperature, volume, pressure, etc. could be generalized to arbitrary nonequilibrium states or not is still unclear. Fortunately, the situation is quite different when we study the master-equation processes, in which the state variables are just their transient distributions and specific time-dependent transition laws.

However, the notation of internal energy seems unable to be directly generalized to arbitrary state, and the First Law of Thermodynamics remains unknown. In the present article, we will show that there does exist an obvious way to generalize it to the time-dependent Markov processes, enlightened by the mathematical equivalence of Jarzynski and Hatano-Sasa equalities [26, 33].

In the present article, we only investigate the isothermal system with fixed temperature \( T \). The role of temperature here is simply to keep the environment constant, therefore we did not have to be so careful about precise parameterization of the temperature. We simply used the same temperature scale as the heat baths, and declared that the temperature may be measured by a thermometer, just as Sasa claimed in his recent review [34].

1. Gibbs entropy postulate and its generation

Unlike the traditional approach of equilibrium thermodynamics, we should start with the general definition of entropy, and then turn back to consider the existence of internal energy. The common definition of Gibbs entropy associated with any discrete probability distribution \( \{ p_i \} \) is

\[
S(\{ p_i \}) = -k \sum_i p_i \log p_i,
\]

where \( k \) is the Boltzmann constant.

In statistical mechanics, it gives the entropy for a canonical ensemble of a molecular system at constant temperature, and is a generalization of Boltzmann’s formula to a situation with nonuniform probability distribution.

Denote the real distribution at time \( t \) is \( p(t) = \{ p_i(t) \} \), and we define the general entropy at time \( t \) as \( S(t) = -k \sum p_i(t) \log p_i(t) \).

It is widely known that the entropy change \( dS \) could be to distinguished in two terms [4, 1, 55]; the first, \( d_sS \) is the transfer of entropy across the boundaries of
the system, and the second $d_iS$ is the entropy produced within the system.

Here, it is easy to derive that

$$\frac{dS(t)}{dt} = d_iS + d_eS = epr(t) - hdr(t),$$

(2)

where

$$epr(t) = d_iS = \frac{1}{2} \sum_{i,j} (p_i(t)q_{ij}(t) - p_j(t)q_{ji}(t)) \log \frac{p_i(t)q_{ij}(t)}{p_j(t)q_{ji}(t)}$$

is just the instantaneous entropy production rate [30], and

$$hdr(t) = d_eS = \frac{1}{2} \sum_{i,j} (p_i(t)q_{ij}(t) - p_j(t)q_{ji}(t)) \log \frac{q_{ij}(t)}{q_{ji}(t)}$$

is due to the exchange of heat with the exterior, called the heat dissipation rate.

2. Entropy production along a stochastic trajectory

A trajectory point of view will help us to realize the stochastic nature of kinetics profoundly. Regarding its stochastic nature, any individual particle of the ensemble is governed entirely by the transition density $Q(t)$ of the system, and ensemble properties depend on their statistics.

We write the trajectory (sample path) of the Markov chain as $X(t)$. Denote by $n_T$ the number of times that $X$ jumps in the time interval $[0, T]$. Let $T_0 = 0$, $T_1 = \inf \{ t > 0 : X(t) \neq X(0) \}$, $T_k = \inf \{ t > T_{k-1} : X(t) \neq X(T_{k-1}) \}$, and $T_{n_T + 1} = T$ be the jumping times.

Seifert [22] defined the sample trajectory entropy along the trajectory at time $t$ as $S(X(t), t) = -k \log p(X(t), t)$, recalling $p(t)$ is the real distribution of the Markov chain $\{X(t)\}$ at time $t$.

The equation for the motion of $S(X(t), t)$ becomes

$$\frac{dS(X(t), t)}{dt} = epr(X(t), t) - hdr(X(t), t),$$

where

$$epr(X(t), t) = -k \frac{\partial \log p(X(t), t)}{\partial t} - k \sum_{T_k} \delta_{t=T_k} \log \frac{p_X(T_k)q_X(T_k)X(T_{k-1})}{p_X(T_{k-1})q_X(T_{k-1})X(T_k)}(t)$$

is the sample entropy production at time $t$, and

$$hdr(X(t), t) = -k \sum_{T_k} \delta_{t=T_k} \log \frac{q_X(T_k)X(T_{k-1})}{q_X(T_{k-1})X(T_k)}(t)$$

is the sample heat dissipation in the medium.

The rationality after these identifications for the change rate of entropy becomes clear when averaging over all the trajectories, then one gets $epr(t) = \langle epr(X(t), t) \rangle$ and $hdr(t) = \langle hdr(X(t), t) \rangle$.

It is also pointed out by Seifert [22] that the trajectory-dependent entropy of the particle could be measured experimentally for a time-dependent protocol by first recording over many trajectories the probability distribution $p_i(t)$, from which the entropy of each trajectory can be inferred.

3. Decomposition of heat conduction

The idea of decomposing the total heat into a “housekeeping” part and another “excess” part was put forward by Oono and Paniconi [3], and made explicit in Langevin systems by Hatano and Sasa [22].

The sample heat dissipation $hdr(X(t), t)$ could be regarded as the total heat conduction $Q_{tot}(X(t), t)$ with the medium, i.e.

$$Q_{tot}(X(t), t) = T \cdot hdr(X(t), t),$$

and its ensemble average $Q_{tot}(t) = T \cdot hdr(t)$. By convention, we take the sign of heat to be positive when it flows from the system to the heat bath.

For any fixed $t$, there is a steady distribution $\pi(t) = \{ \pi_i(t) \}$ corresponding to $Q(t)$ satisfying $\pi(t)Q(t) = 0$, which need not obey the detailed balance condition $\pi_i(t)q_{ij}(t) = \pi_j(t)q_{ji}(t)$.

Then we could define the other two kinds of heat: the housekeeping heat and excess heat along the trajectory [22, 26, 33, 34, 36, 37]:

$$Q_{hk}(X(t), t) = -kT \sum_{T_k} \delta_{t=T_k} \log \frac{\pi_X(T_k)q_X(T_k)X(T_{k-1})}{\pi_X(T_{k-1})q_X(T_{k-1})X(T_k)}(t),$$

$$Q_{ex}(X(t), t) = kT \sum_{T_k} \delta_{t=T_k} \log \frac{\pi_X(T_k)}{\pi_X(T_{k-1})},$$

and obviously $Q_{tot}(t) = Q_{hk}(X(t), t) + Q_{ex}(X(t), t)$.

After averaging over all the trajectories, one gets

$$Q_{hk}(t) = \frac{1}{2} kT \sum_{i,j} \langle p_i(t)q_{ij}(t) - p_j(t)q_{ji}(t) \rangle \log \frac{\pi_i(t)}{\pi_j(t)}(t),$$

$$Q_{hk}(t) = \frac{1}{2} kT \sum_{i,j} \langle p_i(t)q_{ij}(t) - p_j(t)q_{ji}(t) \rangle \log \frac{\pi_i(t)q_{ij}(t)}{\pi_j(t)q_{ji}(t)},$$

and also $Q_{tot}(t) = Q_{ex}(t) + Q_{hk}(t)$.

More importantly, we found out that the housekeeping heat is always nonnegative, which implies the nonequilibrium essence of the system:
\( Q_{hk}(t) = kT \sum_{i,j} p_i(t)q_{ij}(t) \log \frac{\pi_i(t)q_{ij}(t)}{\pi_j(t)q_{ji}(t)} \)

\[
\geq -kT \sum_{i,j} p_i(t)q_{ij}(t) \left( \frac{\pi_j(t)q_{ji}(t)}{\pi_i(t)q_{ij}(t)} - 1 \right) \\
= -kT \sum_i p_i(t) \sum_j \pi_j(t)q_{ji}(t) + kT \sum_{i,j} p_i(t)q_{ij}(t) \\
= 0,
\]

by making use of a simple inequality \( \log x \leq x - 1 \) for \( x > 0 \), and the identity \( \sum_j q_{ij}(t) = 0 \).

For equilibrium system, \( Q_{ex} \) reduces to the total heat \( Q_{tot} \), because in this case \( Q_{hk} = 0 \) due to \( \pi_i(t)q_{ij}(t) = \pi_j(t)q_{ji}(t) \). And in time-independent steady state, \( Q_{ex}(t) = 0 \), and hence the housekeeping heat \( Q_{hk} \) equals the work done by the external driven force, which is all dissipated \([31,32]\).

However, the situation is quite different for the time-dependent nonequilibrium system, in which the housekeeping heat still comes from the work done by some external driven force but where does the excess heat come from? We will show that its origin is just the change of a thermodynamic quantity called general internal energy.

4. Dissipative work and general internal energy

Notice that the heat conduction only occurs at the specific time when the sample trajectory jumps, but which manner of energy exchange would happen during the time interval as the trajectory stays in the same state? It is surely due to the variation of the time-dependent transition laws from the external perturbation acting on the system. With the classic quantum system in mind, we realize that it is just the “dissipative work” called by Jarzynski and Crooks \([20,21,22,36,37,38]\), and rigorously formulated by Min Qian and the author \([33]\).

The dissipative work along the trajectory is defined as \([23,33,39]\):

\[
W(X(t),t) = -kT \frac{\partial \log \pi_i(t)}{\partial t} \big|_{i=X(t)},
\]

with ensemble average \( W(t) = -kT \sum_i p_i(t) \frac{d \log \pi_i(t)}{dt} \).

If the system satisfies the detailed balance conditions for all time, i.e. \( \pi_i(t)q_{ij}(t) = \pi_j(t)q_{ji}(t) \), then the traditional concept of internal energy exists and both of the excess heat and dissipative work contribute to its change, which is the First Law undoubtedly \([33]\). Therefore, we believe that the situation will not be essentially different even if detailed balance conditions fails.

Further, we find out that the dissipative work subtracting the excess heat along the trajectory does not depend on the particular “path” taking through the parameter space, namely, only depends upon the initial and final states, i.e.

\[
W(X(t),t) - Q_{ex}(X(t),t) = dU(X(t),t),
\]

where \( U(X(t),t) = -kT \log \pi_X(t) \) could be regarded as the internal energy of state \( X(t) \).

Thus, there exactly exists a “general internal energy”

\[
U(t) = \langle U(X(t),t) \rangle = -kT \sum_i p_i(t) \log \pi_i(t),
\]

whose derivative is just the difference of the dissipative work and excess heat, i.e.

\[
\frac{dU(t)}{dt} = -Q_{ex}(t) + W(t).
\]

It is just the ordinary internal energy for the equilibrium canonical ensemble according to the Maxwell-Boltzmann’s law. Hence here Eq.(3) is just the generalized First Law of thermodynamics.

5. General free energy and the concept of free heat

Based on the elementary definition of free energy in equilibrium thermodynamics \( F = U - TS \), we could define a general free energy in the same way:

\[
F(t) = U(t) - TS(t) = kT \sum_i p_i(t) \log \frac{p_i(t)}{\pi_i(t)},
\]

which is just the relative entropy of the distribution \( \{ p_i(t) \} \) with respect to another one \( \{ \pi_i(t) \} \) from the mathematical point of view \([40]\).

For equilibrium system, it is just the Gibbs free energy in a spontaneously occurring chemical reaction at constant pressure \( p \) and temperature \( T \), and also the Helmholtz free energy for systems at constant \( V \) and \( T \) \([41]\). Its change gives the maximum work, other than \( pV \) work. Therefore, it is called a “hybrid free energy” by Ross, J. \([41]\).

More important, Schnakenberg \([14]\) has shown that it is just the Lyapunov function as well as Prigogine-Glansdorff criterion certificating the thermodynamic stability for the steady state of the time-independent master equation system. This will be revisited in Sec. II.C.

Due to the Jensen’s equality for the convex function \(-\log x\), we have \( F(t) \geq 0 \), and the equality holds if and only if \( p_i(t) = \pi_i(t) \), for each state \( i \).

On the other hand,

\[
\frac{dF(t)}{dt} = \frac{dU(t)}{dt} - T \frac{dS(t)}{dt} = W(t) - (T \cdot epr(t) - Q_{hk}(t)),
\]

Here we introduce a new concept named Free heat \( Q_f(t) = T \cdot epr(t) - Q_{hk}(t) \) identifying the free energy change in the form of heat, i.e.

\[
\frac{dF(t)}{dt} = W(t) - Q_f(t).
\]

This concept will play the central role in the extended form of the Second Law of Thermodynamics below.
B. Energy Balance and External Driven Force

The First Law of Thermodynamics is essentially an extension of the principle of the conservation of energy to include systems in which there is flow of heat. But the situation becomes more complicated in nonequilibrium case, since there may exists some external driven force which also pumps energy into the system but does not contribute to the change of internal energy [7].

Denote the work done by the external driven force as $Edf(t)$, and we here try to figure out its relationship with other quantities defined in the previous sections.

According to energy balance, one has

$$W(t) + Edf(t) = \frac{dU(t)}{dt} + T \cdot hdr(t).$$

On the other hand, we have already known that

$$\frac{dU(t)}{dt} = -Q_{ex}(t) + W(t) = -Q_{tot}(t) + Q_{hk}(t) + W(t),$$

and also $Q_{tot}(t) = T \cdot hdr(t)$.

Therefore, it yields $Edf(t) = Q_{hk}(t)$, which is only known to be valid in steady state before.

Now we understand that there exist totally two kinds of external works done on the system, one is the dissipative work $W(t)$ and the other $Edf(t)$ from the external driven force. They result in the change of general internal energy and the heat dissipation respectively.

C. Second Law of Thermodynamics

Traditional Second Law of Thermodynamics has two kinds of statements [42]: The Kelvin-Planck statement “No process is possible whose sole result is the complete conversion of heat into work” and the Clausius statement “No process is possible whose sole result is the transfer of heat from a colder to a hotter body”.

Now, a central problem arises: how does these thermodynamic laws apply to such a nonequilibrium time-dependent process? First, we provide a rigorous quantitative approach to the Clausius inequality and Helmholtz/Gibbs free energy inequalities based on the nonnegativity of entropy production rate for nonequilibrium time-dependent processes.

Then a new concept “instantaneous reversible process” [30] with zero entropy production rate natually emerges, which corresponds to the ideal reversible process involved in the classic theory of equilibrium thermodynamics, and it will imply that there does not exist any real reversible process connecting two different equilibrium states.

Furthermore, an extended quantitative form of Second Law of Thermodynamics will be developed built on the nonnegativity of the new concept “free heat”, which only appears during time-dependent processes and accords well to the phenomenological statement by Oono and Panicini [3].

1. Former quantitative forms of the Second Law

Although all the thermodynamic quantities in the previous sections could be defined along the sample trajectory, the Clausius inequality and many other thermodynamic constrains related to the Second Law should be interpreted statistically through ensemble average.

Notice that every term in the expression of the entropy production rate, i.e.

$$epr(t) = \frac{1}{2} \sum_{i,j} (p_i(t)q_{ji}(t) - p_j(t)q_{ij}(t)) \log \frac{p_i(t)q_{ji}(t)}{p_j(t)q_{ij}(t)}$$

is nonnegative, and the equality holds if and only if $p_i(t)q_{ji}(t) = p_j(t)q_{ij}(t)$ for each pair of states $i$ and $j$.

Then according to Eqs. (2) and (4), we derived several inequalities of the differential forms:

$$T \frac{dS(t)}{dt} + Q_{tot}(t) = T \cdot epr(t) \geq 0, \quad (5a)$$

$$\frac{dF(t)}{dt} - W(t) - Q_{hk}(t) = -T \cdot epr(t) \leq 0. \quad (5b)$$

Eq. (5a) is just the well-known Clausius inequality ($dS \geq -\frac{W}{T}$), which is rectified to obtain expressions for the entropy produced ($dS$) as the result of heat exchanges ($Q_{tot}$). And Eq. (5b) is a general version of the free energy inequality for the amount of work performed on the system, since the work values must then be consistent with the Kelvin-Planck statement [43] and forbids the systematic conversion of heat to work.

More precise, the quantity $Q_{hk}(t)$ in Eq. (5b) vanishes when the detailed balance condition ($\pi_i(t)q_{ji}(t) = \pi_j(t)q_{ij}(t)$) holds and then it returns back to the traditional Helmholtz or Gibbs free energy inequalities of equilibrium thermodynamics depending on whether it is a NVT or NPT system [44]. In this case, $-dF \geq -W$, which implies the decrease of free energy gives the maximum dissipative work done upon the external environment.

Their corresponding integral forms are

$$T \Delta S + \int Q_{tot}(t)dt \geq 0, \quad (6a)$$

$$\Delta F - \int W(t)dt - \int Q_{hk}(t)dt \leq 0. \quad (6b)$$

2. Reversible process

Reversible process that is beneficial for thermodynamic studies, is defined as a process that, once having taken place, can be reversed, and in so doing leaves no change in either the system or surroundings. However, there still leaves a fundamental question: “what is precisely the reversible process that connects two different equilibrium states?” Since it is well-known that “only irreversible
processes contribute to entropy production”, what we need here is only to check the condition for which the entropy production vanishes. Then we find out that it is just equivalent to the concept “instantaneous reversibility” [30], which is a natural generalization of equilibrium state.

For the time-dependent process discussed in the present article, let \( e^{pr}(t) = 0 \) for each time \( t \), then we find that all the steady distributions \( \{\pi(t)\} \) must be independent with time \( t \) (i.e. \( \pi(t) \equiv \text{some fixed distribution} \) \( \pi \) and the detailed balance condition holds, i.e. \( \pi_i q_{ij}(t) = \pi_j q_{ji}(t) \). Therefore, during this process, the transient state at each time \( t \) is the real equilibrium state. As is well known, thermodynamic equilibrium is in general maintained through detailed balance. For equilibrium states, the positivity of entropy production rate and the appearance of circulations [15].

Note that in the stationary time-independent case, the first introduced by Kolmogorov. It has been rigorously proved by Min Qian, Minping Qian and their collaborators that the mathematical essence of these two concepts actually turns out to be the same, and the major characteristic of a nonequilibrium steady state is shown to be the positivity of entropy production rate and the appearance of circulations [12]. But unfortunately it is not true, and this is just why equilibrium thermodynamics could not be directly generalized to the far-from-equilibrium case.

3. Extended quantitative forms of the Second Law

Oono and Paniconi [3] put forward a phenomenological extended form of the Second Law to nonequilibrium steady states, which claims the irreversibility of the process converting work into excess heat when modulo house-keeping heat. After that, a quantitative expression in Langevin systems was given for the transition processes between steady states by Hatano and Sasa [29].

Here we give a rather different but much more general derivation, only need to notice that the free heat \( Q_f(t) = e^{pr}(t) - TQ_{hk}(t) \geq 0 \) again due to the simple inequality \( \log x \leq x - 1 \) for \( x > 0 \):

\[
Q_f(t) = T \cdot e^{pr}(t) - Q_{hk}(t)
\]

\[
= \sum_{ij} p_i(t) q_{ij}(t) \log \frac{p_i(t) \pi_j(t)}{p_j(t) \pi_i(t)}
\]

\[
\geq \sum_{ij} p_i(t) q_{ij}(t) \left( \frac{p_i(t) \pi_i(t)}{p_j(t) \pi_j(t)} - 1 \right)
\]

\[
= \sum_j \pi_j(t) \sum_i p_i(t) q_{ij}(t) - \sum_i p_i(t) \sum_j q_{ij}(t)
\]

\[
= 0,
\]

Then according to Eqs. (2) and (4), we have another group of thermodynamic inequalities in the differential forms:

\[
T \frac{dS(t)}{dt} + Q_{ex}(t) = T \cdot e^{pr}(t) - Q_{hk}(t) \geq 0,
\]

\[
\frac{dF(t)}{dt} - W(t) = -Q_f(t) = -T \cdot e^{pr}(t) + Q_{hk}(t) \leq 0.
\]

followed by their corresponding integral forms

\[
T \Delta S + \int Q_{ex}(t) dt \geq 0,
\]

\[
\Delta F - \int W(t) dt \leq 0.
\]

Eq. (8a) is the extended form of Clausius inequality during any nonequilibrium time-dependent process, whose special case is included in Hatano and Sasa’s work [29]. And Eq. (9a) is a different general form of free energy inequality. It implies the dissipative work value must be consistent with the Oono-Paniconi statement of the extended Second Law of thermodynamics [3], which forbids the systematic conversion of excess heat to work.

For equilibrium case, \( Q_{ex} = Q_{tot} \), then they both return back to Eq. (5a) actually. And then if in steady state, then \( Q_f(t) \equiv 0 \), and this form of the Second Law completely disappears.

III. APPLIED TO CLASSIC THERMODYNAMIC PROCESSES

A. Time-independent case

1. Equilibrium states and nonequilibrium steady states

Here we consider the Markov chain with transition density matrix \( Q = \{q_{ij}\} \) and stationary distribution \( \pi = \{\pi_i\} \) satisfying \( \pi Q = 0 \).

The first step is to distinguish equilibrium and steady nonequilibrium states. As is well known, thermodynamic equilibrium is in general maintained through detailed balance, which was already known by Boltzmann; and the reversibility of a time-independent stochastic process was first introduced by Kolmogorov. It has been rigorously proved by Min Qian, Minping Qian and their collaborators that the mathematical essence of these two concepts actually turns out to be the same, and the major characteristic of a nonequilibrium steady state is shown to be the positivity of entropy production rate and the appearance of circulations [12].

Note that in the stationary time-independent case, the general internal energy, entropy, and free energy are all independent of time, and both of the dissipative work and excess heat vanish. That may be the reason why these concepts have not been found previously, when only dealing with steady states.
For steady states, we have the important relations
\[ T \cdot hdr = T \cdot epr = Q_{hk} = Q_{tot} \geq 0, \]
and the equality holds if and only if at equilibrium states.

Moreover, the energy balance tells us that the external driven force \( Edf = T \cdot hdr \), which implies the external energy pumped in all changes into heat dissipation [6, 35]. And it is also consistent with the truth that there is no external energy source for equilibrium states in which \( hdr \equiv 0 \).

2. Relaxation process towards equilibrium states

Each undriven system will be found to reach a state where no further change takes place and it is then said to have come to thermodynamic equilibrium. In general, the relaxation to thermodynamic equilibrium will involve both thermal and work-like interactions with the surroundings, and then which will occur during this relaxation process?

First, the time-independent property implies the vanishing of dissipative work, i.e. \( W(t) \equiv 0 \), but the excess heat \( Q_{ex}(t) \) may not vanish. Second, since the final state of the relaxation process is at equilibrium, so the external driven force \( Edf(t) \) disappears. Consequently, \( Q_{hk}(t) = Edf(t) \equiv 0 \), and \( Q_{tot}(t) \) reduces to \( Q_{ex}(t) \).

However, it will still dissipate heat and have positive entropy production rate unless it has already arrived at the final equilibrium state. To be more precise, we have \( hdr(t) = \frac{Q_{tot}(t)}{T} = \frac{Q_{ex}(t)}{T} \), therefore,
\[ \frac{dU(t)}{dt} = -Q_{ex}(t) = -T \cdot hdr(t), \]
which is just the First Law of Thermodynamics.

Furthermore,
\[ \frac{dF(t)}{dt} = W(t) - T \cdot epr(t) + Q_{hk}(t) = -T \cdot epr(t) \leq 0, \]
hence \( F(t) \) is just the Lyapunov function while relaxing towards equilibrium states [14]. Until now we know that this Lyapunov function is just a directly corollary of the Second Law.

3. Relaxation process towards steady state

The relaxation process towards steady states has been extensively discussed by Glansdorff and Prigogine [3, 4], and then by Schnakenberg for the master-equation systems [14].

Comparing with the previous discussion on the relaxation process towards equilibrium state, we will show that the sole difference here only stays within the housekeeping heat provided by some specific external driven force.

Here, the First Law of Thermodynamics also becomes
\[ \frac{dU(t)}{dt} = -Q_{ex}(t), \]
and the energy balance reads
\[ \frac{dU(t)}{dt} + T \cdot hdr(t) = Edf(t). \]

Combined with \( Edf(t) = Q_{hk}(t) \), it is found that the whole heat dissipation is from two sources: one is the excess heat contributing to the change of general internal energy; the other is the housekeeping heat caused by the external driven force.

The extended form of the Second Law now reads
\[ \frac{dF(t)}{dt} = -T \cdot epr(t) + Q_{hk}(t) = -Q_{f}(t) \leq 0, \]
thus \( F(t) \) serves as a Lyapunov function for this relaxation process [14], which actually has a solid thermodynamic basis now.

B. Time-dependent case

Time-dependent processes are causing more and more interests from physicists nowadays [23, 24, 45, 46], and it will uncover many important thermodynamic properties that originally hidden behind the stationary time-independent case.

1. Cyclic process

In equilibrium thermodynamics, a thermodynamic cycle is a series of thermodynamic processes which returns a system to its initial state. As a conclusion of cyclic process, all the state variables should have the same value as they had at the beginning. Thus \( \Delta U = \Delta S = \Delta F = 0 \).

But variables such as heat and work are not zero over a cycle, but rather are process dependent. The First Law of Thermodynamics dictates that the net heat input is equal to the net work output over any cycle, i.e. \( \int W(t)dt = \int Q_{tot}(t)dt \).

Hence in this case, the former form of the Second Law [6] gives
\[ \int Q_{tot}(t)dt = T \cdot \int epr(t)dt \geq 0, \tag{12a} \]
\[ \int W(t)dt \geq -\int Q_{hk}dt. \tag{12b} \]

If one rewrite Eq. \( \tag{12a} \) as \( \int (W(t) + Edf(t))dt = \int Q_{tot}(t)dt \geq 0 \), then it is just the familiar statement of traditional Second Law of Thermodynamics “the conversion from work to total heat is irreversible”.

Moreover, the extended form [9] says
\[ \int Q_{ex}(t)dt = \int Q_f(t)dt \geq 0, \quad (13a) \]
\[ \int W(t)dt = \int Q_{ex}(t)dt \geq 0, \quad (13b) \]
confirming the claim that “the conversion from work to excess heat is irreversible” [5]. In other words, during a cyclic process, not only the total heat but also the excess heat could only be from the system into the heat bath rather than follow the opposite direction.

2. Transitions between equilibrium states

Jarzynski provided an expression for the equilibrium free energy difference between two configurations of a system, in terms of an ensemble of finite-time measurements of the work performed through switching from one configuration to the other (See a recent review [45] and references in).

In the stochastic-process approach [21, 26, 32], we consider the transition between two equilibrium states realized in the time interval \([0, T]\) where the detailed balance condition is satisfied. In other words, there is no external driven force, i.e. \(Edf(t) = Q_{he}(t) \equiv 0\).

Then the energy balance becomes
\[ W(t) = \frac{dU(t)}{dt} + T \cdot hdr(t), \]
thus one could realize that it is not very reasonable to call the quantity \(W(t)\) as “dissipative”, since part of it would be stored in the general internal energy rather than really convert into heat.

Notice that when one finishes the task of driving the process from time 0 to time \(T\) through modulating the time-dependent transition density matrix \(Q(t)\) (denoted as process 1), the system has not reached the final equilibrium state yet. Then we should wait until it really arrives (denoted as process 2), which is just the “relaxation process towards equilibrium state” with the fixed transition density \(Q(T)\) described in the previous subsections.

According to Eq. (13), we have
\[ \Delta F_1 \leq \int W(t)dt, \quad \text{and} \quad \Delta F_2 \leq \int W(t)dt \] for process 1 and 2 respectively.

Finally, since \(\int W(t)dt = 0\), and \(\Delta F = \Delta F_1 + \Delta F_2\) is just the free energy difference between the initial and final equilibrium states, we conclude \(\Delta F \leq \int W(t)dt\). It is just why we could neglect process 2 when applying Jarzynski’s work relation in experiments.

Note that the situation is quite different when regarding Hatano-Sasa’s equality for transitions between steady states [23]. It has not been explicitly pointed out in previous works [23, 26, 33, 45]. See below for details.

3. Transitions between steady states

The main contribution of Hatano and Sasa [23, 34] is to give the first explicit expression for the extended form of the Second Law put forward by Oono and Paniconi [3], during the transition process between steady states. They also found out a general definition of entropy enlighten from the idea that any proper formulation of steady state thermodynamics should reduce to equilibrium thermodynamics in the appropriate limit, so that \(Q_{ex}\) should correspond to the change of a generalized entropy \(S\).

However, what they defined is just the general internal energy consistent with the First Law of Thermodynamics rather than the general Gibbs entropy in the present article and also in Seifert’s recent work [27]. Note that the two quantities are always different except for steady states, hence the extend form of Second Law of thermodynamics during the course of transition between two steady states derived by Hatano and Sasa is not flawed.

Similar to the preceding transition process between two equilibrium states, when one finishes driving the process from time 0 to \(T\) (also denoted as process 1) through varying the time-dependent transition density \(Q(t)\), the system has not reached the final steady state yet, and we should wait until it arrives (denoted as process 2), which is just the “relaxation process towards steady state” where the transition density is fixed at \(Q(T)\).

According to Eq. (10), we get
\[ \int Q_{ex}(t)dt \geq -\Delta S_1, \quad \text{and} \quad \int Q_{ex}(t)dt \geq -\Delta S_2 \] for process 1 and 2 respectively.

Finally, since \(\Delta U = \Delta S = \Delta S_1 + \Delta S_2\) representing the energy (entropy) difference between the initial and final steady states, we derive that
\[ \int Q_{ex}(t)dt = \int Q_{ex}(t)dt + \int Q_{ex}(t)dt \geq -\Delta S. \]

Hatano and Sasa [23] concluded that the equality held for an infinitely slow operation in which the system is in a steady state at each time during a transition (“slow process”).

It is indispensable to emphasize that we could not neglect process 2 this time when applying Hitano-Sasa’s identity, because here \(\int Q_{ex}(t)dt\) may not be zero, which implies that the relaxation process towards the final steady state will also contribute to the heat dissipation. This critique has already be pointed out by Cohen and Mauzerall [47], but unfortunately what they criticized is the Jarzynski’s equality rather than Hatano-Sasa equality. In real experiment, this relaxation process may be rapid enough and could somehow be omitted.

C. Summary

The essential difference between these typical processes relies mainly on the signs of the three key thermodynamic
quantities: the housekeeping heat, entropy production and free heat. And also the dissipative work would disappear for time-independent processes. See Tab. I for details.

IV. DISCUSSION

It is the main thesis of this article that we are only at the beginning of a new development of theoretical chemistry and physics in which thermodynamic concepts may play an even more basic role. “In any case, the number of thermodynamic or macroscopic variables is much less than the large number of the microscopic degrees of freedom. Hence, the transition from a microscopic to a macroscopic description involves a drastic reduction of the information about the system.”

However, the study of thermodynamics before is largely confined to equilibrium states. Although the field of “nonequilibrium thermodynamics” has successfully extended the 19th century concepts of equilibrium thermodynamics to the systems that are close to, or near equilibrium, the understanding of far-from-equilibrium systems is still poor.

To investigate these points, stochastic thermodynamics has stepped much further than other approaches during the last two decades. For stochastic systems, the central problem is around the extension of the Second Law, which originally describes the fundamental limitation on possible transitions between equilibrium states. And recently, it has been studied from the trajectory point of view, which stimulated the rapid emergence of so-called fluctuation theorems. Most of them are merely valid for specific processes, such as steady states or transitions between steady states; while the newly developed integral fluctuation theorems for total entropy production and housekeeping heat could hold for arbitrary time-dependent systems.

These fluctuation theorems require the definitions of thermodynamic functionals along the trajectory, and most of the have already done. Thus the main purpose of the present article is to investigate the thermodynamic laws within them, especially the two quantitative forms of the Second Law.

Based on the stochastic processes, we put forward a rather relatively integral theory of nonequilibrium thermodynamics, which may be more definite and convincing but more restrictive than the previous phenomenological frameworks. In addition, it would be interesting to test experimentally all the quantities and relations, especially in nonharmonic time-dependent potentials, where one does not expect Gaussian distributions.

Acknowledgments

The author is grateful to Prof. Min Qian in Peking University and Prof. Hong Qian in University of Washington for helpful discussions.

[1] Haken, H.: Synergetics: an introduction: nonequilibrium phase transitions and self-organization in physics, chemistry, and biology. Berlin, New York: Springer-Verlag 1977
[2] Haken, H.: Advanced synergetics: instability hierarchies of self-organizing systems and devices. Berlin, New York: Springer-Verlag 1983
[3] Glansdorff, P. and Prigogine, I.: Thermodynamic theory of structure, stability and fluctuations. London: Wiley-Interscience 1971
[4] Nicolis, G. and Prigogine, I.: Self-organization in nonequilibrium systems: from dissipative structures to order through fluctuations. New York: Wiley 1977
[5] Oono, Y. and Paniconi, M., Prog. Theor. Phys. Suppl. 130, 29 (1998)
[6] Qian, H., J. Phys. Condens. Matter 17, S3783 (2005)
[7] Qian, H. and Beard, D.A., Biophys. Chem. 114, 213 (2005)
[8] Oussargr, L. and Machlup, S., Phys. Rev. 91, 1505 (1953)
[9] Machlup, S. and Oussargr, L., Phys. Rev. 91, 1512 (1953)
[10] Hill, T.L., J. Theoret. Biol. 10, 442 (1966)
[11] Hill, T.L.: Free energy transduction in biology. New York: Academic Press 1977
[12] Hill, T.L.: Free energy transduction and biochemical cycle kinetics. New York: Springer-Verlag 1989
[13] Hill, T. and Chen, Y., Proc. Nat. Acad. Sci. USA 72, 1291 (1975)
[14] Schnakenberg, J., Rev. Modern Phys. 48(4), 571 (1976)
[15] Jiang, D.Q., Qian, M. and Qian, M.P.: Mathematical theory of nonequilibrium steady states - On the frontier of probability and dynamical systems. (Lect. Notes Math. 1833) Berlin: Springer-Verlag 2004
[16] Evans, D.J., Cohen, E.G.D. and Morriss, G.P., Phys. Rev. Lett. 71, 2401 (1993)
[17] Ge, H. and Jiang, D.Q., J. Phys. A 40 F713 (2007)
[18] Kurchan, J., J. Phys. A: Math. Gen. 31, 3719 (1998)
[19] Lebowitz, J.L. and Spohn, H., J. Stat. Phys. 95, 333 (1999)
[20] Jarzynski, C., Phys. Rev. Lett. 78, 2690, (1997)
[21] Jarzynski, C., Phys. Rev. E 56, 5018, (1997)
[22] Jarzynski, C., J. Stat. Phys. 96, 415 (1999)
[23] Hatano, T. and Sasa, S., Phys. Rev. Lett. E. 86, 3463 (2001)
[24] de Groot, S. R. and Mazur, P.: Non-equilibrium thermodynamics North-Holland 1962
[25] Seifert, U., Phys. Rev. Lett. 95, 040602 (2005)
[26] Ge, H. and Jiang, D.Q., J. Stat. Phys. 131 675 (2008)
[27] Ge, H.: Nonequilibrium thermodynamics of time-dependent Langevin systems: Energy balance relation ang the extended form of the second law. (arXiv: 0904.2059)
[28] Fall, C.P., Marland, E.S., Wagner, J.M. and Tyson, J.J.: Computational cell biology. New York: Springer-Verlag 2002
TABLE I: The signs of important thermodynamic quantities. Process 1: Equilibrium state; Process 2: Nonequilibrium steady state; Process 3: Relaxation process towards equilibrium state; Process 4: Relaxation process towards nonequilibrium steady state; Process 5: Transition between equilibrium states; Process 6: Transition between steady states. "0" for zero, "+" for positive, "-" for negative, and "?" for uncertainty.

| Process   | Process 1 | Process 2 | Process 3 | Process 4 | Process 5 | Process 6 |
|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Dissipative work | 0         | 0         | 0         | 0         | ?         | ?         |
| Excess heat | 0         | 0         | ?         | ?         | ?         | ?         |
| Housekeeping heat | 0         | ?         | 0         | +         | 0         | +         |
| Entropy production | 0         | +         | +         | +         | +         | +         |
| Free heat | 0         | 0         | +         | +         | +         | +         |

[29] Kolomeisky, A.B. and Fisher, M.E.: Molecular motors, *Annu. Rev. Phys. Chem.* 58 675 (2007)
[30] Ge, H., Jiang, D.Q. and Qian, M., *J. Appl. Prob.* 43(4) 1028 2006
[31] McQuarrie, D.A., *J. Appl. Prob.* 4(3), 413 (1967)
[32] Qian, H. and Elson E.L., *Biophys. chem.* 101-102 565 (2002)
[33] Ge, H., and Qian, M., *J. Math. Phys.* 48 053302 (2007)
[34] Sasa, S. and Tasaki, H., *J. Stat. Phys.* 125, 125 (2006)
[35] Qian, H., *J. Chem. Phys.* 110, 15063 (2006)
[36] Crooks, G.E., *J. Stat. Phys.* 90, 1481 (1998)
[37] Crooks, G.E., *Phys. Rev. E* 60, 2721 (1999)
[38] Crooks, G.E., *Phys. Rev. E* 61(3), 2361 (2000)
[39] Hummer, G. and Szabo, A., *Proc. Nat. Acad. Sci. USA* 98(7), 3658 (2001)
[40] Qian, H., *Phys. Rev. E* 63, 042103 (2001)
[41] Ross, J.: *Thermodynamics and fluctuations far from equilibrium.* Springer-Verlag Berlin Heidelberg 2008
[42] Adkins, C.J.: *Equilibrium Thermodynamics*, 3rd edn. (Cambridge University Press) 1983
[43] Finn, C.B.P.: *Thermal Physics*, 2nd edn. (Chapman and Hall, London) 1993
[44] Beard, D.A. and Qian, H.: *Chemical Biophysics: Quantitative analysis of cellular systems.* (Cambridge University Press) 2008
[45] Jarzynski, C., *Eur. Phys. J. B* 64 331 (2008)
[46] Zubarev, D.N.: *Nonequilibrium statistical thermodynamics* Consultants Bureau 1974
[47] Cohen, E.G.D. and Mauzerall, D., *J. Stat. Mech.: Theor. Exp.* P07006 (2004)
[48] Schnakenberg, J.: *Thermodynamic Network Analysis of Biological Systems.* Springer-Verlag, Berlin Heidelberg 1977
[49] Mou, C.Y., Luo, J.L. and Nicolis, G., *J. Chem. Phys.* 84, 7011 (1986)
[50] Schmiedl, T. and Seifert, U., *J. Chem. Phys.* 126, 044101 (2007)
[51] Seifert, U., *Eur. Phys. J. B* 64, 423 (2008)
[52] Speck, T. and Seifert, U., *J. Phys. A: Math. Gen.* 38, L581 (2005)