Stochastic Free Energies, Conditional Probability and Legendre Transform for Ensemble Change

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Abstract

This work extends a recently developed mathematical theory of thermodynamics for Markov processes with, and more importantly, without detailed balance. We show that the Legendre transform in connection to ensemble changes in Gibbs’ statistical mechanics can be derived from the stochastic theory. We consider the joint probability \( p_{XY} \) of two random variables \( X \) and \( Y \) and the conditional probability \( p_{X|Y=y^*} \), with \( y^* = \langle Y \rangle \) according to \( p_{XY} \). The stochastic free energies of the \( XY \) system (fluctuating \( Y \) ensemble) and the \( X|Y \) system (fixed \( Y \) ensemble) are related by the chain rule for relative entropy. In the thermodynamic limit, defined as \( V,Y \to \infty \) (where one assumes \( Y \) as an extensive quantity, while \( V \) denotes the system size parameter), the marginal probability obeys \( p_Y(y) \to \exp(-V\phi(z)) \) with \( z = y/V \). A conjugate variable \( \mu = -\phi(z)/z \) naturally emerges from this result. The stochastic free energies of the fluctuating and fixed ensembles are then related by \( F_{XY} = F_{X|Y=y^*} - \mu y^* \), with \( \mu = \partial F_{X|Y=y^*}/\partial y \). The time evolutions for the two free energies are the same: \( d[F_{XY}(t)]/dt = \partial[F_{X|Y=y^*(t)}(t)]/\partial t \). This mathematical theory is applied to systems with fixed and fluctuating number of identical independent random variables (idea gas), as well as to microcanonical systems with uniform stationary probability.

PACS numbers: 05.70.Ln, 02.50.Ey, 82.20.Uv, 89.70.Cf

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I. INTRODUCTION

Recently, a rather complete statistical thermodynamic structure for general Markov dynamics has been revealed \[1-4\]. This formalism provides a novel perspective to investigate the dynamics of Markov processes in terms of two emergent quantities, entropy and free energy, which satisfy certain inequalities \[5\]. It has been shown that the entropy production of a Markov dynamics can be mathematically decomposed into two non-negative terms: free energy dissipation corresponding to Boltzmann’s original idea of irreversibility of spontaneous change, and house-keeping heat (the energy input necessary to keep a system’s stationary state away from equilibrium), corresponding to Brussels school’s notion of irreversibility in nonequilibrium steady states (NESS) \[6-9\]. The stochastic free energy also has another important property: It is conserved in one-to-one invertible dynamics, e.g., diffeomorphism, but decreasing in either many-to-one endomorphism or random dynamics \[10, 11\], with uncertainties either in the past or in the future. This last result has been associated with the Second Law of Thermodynamics \[12, 13\].

Studies on this thermodynamic structure with respect to multiscale dynamics have shown that with time scale separation in coarse-graining, the non-equilibrium stochastic free energy is invariant across different scales, while the entropy increases with finer scales \[14, 15\]. Recall that the “partition function invariance” across scales in term of conditional free energy (potential of mean force) is an essential feature of equilibrium statistical mechanics \[16\]. Note as well that the Bogoliubov inequality—which states that a true free energy is never greater than the free energy of a trial Hamiltonian—corresponds to the information Jensen’s inequality for two random variables \(X\) and \(Y\) with probability distributions \(f_X(x)\) and \(f_Y(x)\) \[11\]: \(\langle \ln f_X(X) \rangle \geq \langle \ln f_Y(X) \rangle\). This also means that \(\langle \ln(f_X(X)/f_Y(X)) \rangle > 0\), the left-hand-side of which is known as relative entropy, or Kullback-Leibler divergence \[11\].

One of the most important results of J.W. Gibbs’ statistical thermodynamic theory, based on various ensembles with different environmental constraints, is the “equivalence” of ensembles as analytical devices for the thermodynamics of the same macroscopic system. For example, the canonical ensemble with fixed \(N\) and \(V\) (\(N\) being the number of particles and \(V\) the volume of a system), the grand canonical ensemble with fixed \(\mu\) (the chemical potential of a particle reservoir) and \(V\), and the isobaric ensemble with fixed \(N\) and pressure over the system \(p\), all give the same macroscopic thermodynamic laws \[17, 18\], including the Maxwell...
relations. Still, for different ensembles, the corresponding thermodynamic potentials, the “free energies” for the Second Law, are different: entropy for the microcanonical ensemble, Helmholtz free energy for the canonical ensemble, Gibbs free energy for the isobaric ensemble, etc. The different thermodynamic potentials are related via Legendre transforms. However, their change in an irreversible process is the same entropy production which underlies the Second Law.

In the present work we expand upon this thermodynamic formalism for Markov processes to include the notion of ensemble change à la Gibbs. The fluctuations in various ensembles with different environmental constraints are certainly different [19, 20]. This indicates that, on a mesoscopic level (e.g. in “nanothermodynamics” [21]), the finite-size effect has to play a certain role in the thermodynamics of small systems [22, 23]. One long noted phenomenon associated with this effect is the “entropy-enthalpy compensation” among different ensembles [19, 20, 24]. Such compensation seems to play a fundamental role in systems with multiscale dynamics [14]. Taking this into account, the present paper aims at studying the relation between different forms of stochastic free energy associated with different stochastic systems, and the rule for their transformation based on two key notions: conditional probability and thermodynamic limit. In fact, one is able to mathematically derive the well-known Legendre transform [25] in Gibbs’ theory. We also show that while the forms of the nonequilibrium stochastic free energy for different ensembles are different, their time evolutions are the same. Attempts had been made previously to show the equivalence of ensembles in NESS Markov processes from a statistical perspective [26, 27], but to our knowledge this is the first time that it is done from the standpoint of irreversible Markovian thermodynamics. We also apply the general mathematical result to the transformation of free energies of different ensembles, e.g., grand canonical [28, 29] and microcanonical Markov systems.

II. STOCHASTIC FREE ENERGY AND CONDITIONAL PROBABILITY

We consider a Markov system with joint discrete random variables $X$ and $Y$ with probability mass function $p_{XY}(m,N,t) = \Pr\{X_t = m, Y_t = N\}$. This can be very general. One particular example, however, could be a system consisting of an arbitrary number of particles, or subsystems, each of which can be in $M$ different states, numbered $1, \ldots, M$. Every particle can jump among all the available states following a continuous-
time, Markovian stochastic process. Let \( Y_t \) be the number of particles at time \( t \) in the system and \( \vec{X}_t = \left( X_t^{(1)}, \cdots, X_t^{(i)}, \cdots, X_t^{(M)} \right) \) be the corresponding particle composition: 
\[ X_t^{(1)} + \cdots + X_t^{(i)} + \cdots + X_t^{(M)} = Y_t. \]
The time evolution of the system corresponds to that of an irreducible continuous-time Markov process for non-negative integer-valued random variables \((\vec{X}, Y)_t\), with joint probability mass function 
\[ p_{XY}(\vec{m}, N, t) = \Pr\{\vec{X}_t = \vec{m}, Y_t = N\}. \]
Without introducing ambiguity, we shall drop the vector notation from \( \vec{X} \) and \( \vec{m} \).

According to [1], the stochastic free energy of the “fluctuating ensemble” with fluctuating \( X \) and \( Y \) is:
\[
F_{\text{flu.ens.}}(t) = \sum_{N=0}^{\infty} \sum_{m=0}^{\infty} p_{XY}(m, N, t) \ln \left[ \frac{p_{XY}(m, N, t)}{p_{XY}^{ss}(m, N)} \right]
\]
\[
= \sum_{N=0}^{\infty} p_Y(N, t) \sum_{m=0}^{\infty} p_X(m, t|N) \ln \left[ \frac{p_X(m, t|N)}{p_X^{ss}(m|N)} \right]
\]
\[ + \sum_{N=0}^{\infty} p_Y(N, t) \ln \left[ \frac{p_Y(N, t)}{p_Y^{ss}(N)} \right], \tag{1} \]
where \( p_{XY}^{ss}(m, N) \) is the unique stationary distribution of the Markov system [30]. Eq. (1) is well-known in probability and information theory as the “chain rule for relative entropy” [7, 11, 12]. The stochastic free energy for the “fixed ensemble” with fluctuating \( X \) but fixed \( Y_t = N \) is:
\[
F_{\text{fix.ens.}}(t|N) = \sum_{m=1}^{\infty} p_X(m, t|N) \ln \left[ \frac{p_X(m, t|N)}{p_X^{ss}(m|N)} \right]. \tag{2} \]
We are interested in the relationship between \( F_{\text{flu.ens.}}(t) \) with mean value
\[
N^*(t) = \sum_{N=0}^{\infty} \sum_{m=0}^{\infty} N p_{XY}(m, N, t), \tag{3} \]
and \( F_{\text{fix.ens.}}(t|N) \) with fixed \( N = N^*(t) \). In Gibbs’ ensemble theory, they correspond to an ensemble change; e.g. grand-canonical to canonical ensembles (by fixing number of particles), canonical to microcanonical ensembles (by fixing the energy), and isobaric to canonical (by fixing the volume). We shall adopt the terminology of grand canonical ensemble in the rest of the paper, with \( X \)’s being number of particles. The mathematics are the same if the \( X \)’s represent energies, volumes, etc., as long as \( Y \) is an extensive quantity.

**Thermodynamic limit.** By \( Y \) being an extensive quantity, we mean that the system has a natural parameter \( V \) such that \( Y \) scales with \( V \). In many applications, this parameter can be the size of a system in terms of total numbers, spatial volumes, etc. The thermodynamic limit is then defined through the system’s size \( V \) and the random variable \( Y \). Both
\( V \) and \( Y \) are extensive quantities and they tend to infinity, while \( Y/V \) becomes an intensive quantity and remains finite. Assuming the large deviation principle, one can assert that in the thermodynamic limit there exists a function \( \phi(z,t) \), \( z = N/V \), such that (see [31, 32] and references therein, as well as [33]):

\[
p_Y(N,t) \sim e^{-V\phi(z,t)}. \tag{4}
\]

It is important to emphasize at this point that we assume the existence of the thermodynamic limit, as well as the validity of the large deviation principle. The novelty of the present work is to show that Gibbs’ Legendre transform is a consequence of the stochastic free energy and the conditional probability.

There are two scenarios that require separated treatments: (i) \( V \to \infty \) first with finite time \( t < T \), for a given \( T \); and (ii) \( t \to \infty \) first with finite \( V \). In the “finite-time scenario” (i), the stochastic dynamics is essentially “trapped” in a local basin of attraction depending upon its initial condition; there is a broken ergodicity since the mean time for transition into another basin of attraction is on the order of \( e^{\alpha V} \) with \( \alpha > 0 \) [34]. In (ii), the system is always ergodic and only the global minimum of \( \phi(z,\infty) \) is relevant for a large system. Furthermore, except at critical conditions of phase transition, the function \( \phi(z,\infty) \) has a unique global minimum, \( \hat{z} \), to which \( Vp_Y(Vz,\infty) \) will converge with probability 1: \( Vp_Y(Vz,\infty) \to \delta(z - \hat{z}) \). Therefore, we can assume without loss of generality that, in both cases, \( \phi(z,t) \) has a single global minimum \( z^*(t) \) for any given \( t \). This means that \( p_Y(N,t) \) has a single dominant maximum at \( N^*(t) = Vz^*(t) \). From these considerations, we expect the distribution \( p_Y(N,t) \simeq 0 \) for most \( N \) values except in the neighbourhood of \( N^* \). For example, a Poisson distribution, in the limit of large \( N^* \), has \( p_Y(N,t) \simeq 0 \) for most \( N \) values, except for those in the range \([N^* - \gamma\sqrt{N^*}, N^* + \gamma\sqrt{N^*}]\), where \( \gamma > 0 \) is a fixed constant. Therefore we have

\[
\sum_{N=0}^{\infty} p_Y(N,t) F_{\text{fix.ens.}}(t|N) = F_{\text{fix.ens.}}(t|N^*(t)). \tag{5}
\]

This is known as the “maximum term method” in classical statistical mechanics [35]. Similarly, one also has that

\[
\sum_{N=0}^{\infty} p_Y(N,t) \ln \left[ \frac{p_Y(N,t)}{p_Y^{ss}(N)} \right] \simeq -\ln p_Y^{ss}(N^*(t)) \tag{6}
\]
in the limit of large \( N^* \), provided that \( p_Y(N,t) \) and \( p_Y^{ss}(N) \) can be approximated by Poisson distributions (see Appendix A). Therefore, we have from Eqs. (5) and (6) that

\[
F_{\text{flu.ens.}}(t) = \sum_{N=0}^{\infty} p_Y(N,t) F_{\text{fix.ens.}}(t|N) + \sum_{N=0}^{\infty} p_Y(N,t) \ln \left( \frac{p_Y(N,t)}{p_Y^{ss}(N)} \right) 
\]

\[
\simeq F_{\text{fix.ens.}}(t|N^*(t)) - \ln p_Y^{ss}(N^*(t)).
\]

Noting that \( p_Y^{ss}(N) = e^{-V \phi(z)} \) is a probability distribution function, where \( \phi(z) \) stands for \( \phi(z,\infty) \), and denoting \( z^* = N^*(t)/V \), then Eq. (7) becomes,

\[
F_{\text{flu.ens.}}(t) = F_{\text{fix.ens.}}(t|N^*) - N^* \mu(z^*),
\]

where

\[
\mu(z) = -\phi(z)/z.
\]

The emergent quantity \( \mu \) is considered to be the conjugate variable to \( N \).

We now apply large deviation theory to show that equation (8) corresponds to a Legendre transform. Observe that the lhs of Eq. (8) has no explicit dependence upon \( V \). Hence, \( \mu(z^*) \) should be chosen in such a way that

\[
\frac{\partial}{\partial V} [F_{\text{fix.ens.}}(t|Vz) - Vz \mu(z)] = 0.
\]

That is,

\[
\frac{\partial F_{\text{fix.ens.}}(t|N)}{\partial N} - \mu(z) = 0.
\]

Therefore,

\[
\begin{align*}
F_{\text{flu.ens.}}(t) &= F_{\text{fix.ens.}}(t|N^*(t)) - N^*(t) \mu(z^*), \\
\mu(z^*) &= \frac{\partial}{\partial N} F_{\text{fix.ens.}}(t|N^*(t)).
\end{align*}
\]

Neglecting the time \( t \), this equation corresponds to the Legendre transform in classic thermodynamic theory.

The sign of \( \mu \). As a large deviation rate function, \( \phi(z) \) is non-negative and its global minimum is at \( \hat{z} \) where \( d\phi(\hat{z})/dz = \phi(\hat{z}) = 0 \). Thus, \( d\mu(\hat{z})/dz = \mu(\hat{z}) = 0 \). If the random variables \( X \)'s are non-negative, so is the random variable \( Y \). Then \( z \) is positive and \( \mu \) in Eq. (9) is a non-positive quantity. For instance, if we consider \( F_{\text{fix.ens}} \) and \( F_{\text{flu.ens}} \) in Eq.
to respectively be the negative entropy and the Helmholtz free energy divided by the
temperature, then \(N^*\) is the internal energy and \(\mu\) is the negative reciprocal temperature
in classical thermodynamics. The relation between this mathematical result and the Third
Law of Thermodynamics remains to be elucidated.

**Time evolution of the free energy.** Eq. (12) also gives

\[
\frac{d}{dt}F_{flu.ens.}(t) = \left[ \frac{\partial F_{fix.ens.}(t|N^*(t))}{\partial t} \right]_{N^*}.
\]  

(13)

We see that even though the two free energies are different for different ensembles, their
time derivative is identical. This is the Brussels school’s insight: “even though there are
different thermodynamic potentials for the Second Law for different ensembles, there is a
unique entropy production.”

**Maxwell relations.** With the introduction of \(\mu(z)\) in Eq. (12), one can obtain several
Maxwell relations. Assume that \(F_{fix.ens}(t|N)\) is also a function of a second thermodynamic
variable \(\xi\): \(F_{fix.ens}(t|N, \xi)\). Then, one immediately gets:

\[
\left( \frac{\partial \mu}{\partial \xi} \right)_N = \left( \frac{\partial^2 F_{fix.ens}}{\partial \xi \partial N} \right) = \left( \frac{\partial \psi}{\partial N} \right)_\xi,
\]

(14)

where \(\psi = (\partial F_{fix.ens}/\partial \xi)_N\) is the thermodynamic conjugate of \(\xi\) in a fixed \(N\) ensemble. For
example, if \(F\) is the Helmholtz free energy and \(\xi\) is the temperature \(T\), then \(-\psi\) is \(S\), the
entropy. Furthermore, we get from Eq. (14) the following relation for the partial molar
entropy:

\[
-\left( \frac{\partial \mu}{\partial T} \right)_N = \left( \frac{\partial S}{\partial N} \right)_T.
\]

(15)

**III. ENTROPY: ITS CHAIN RULE AND TIME EVOLUTION**

Entropy also follows a chain rule with conditional probability [11]:

\[
S_{flu.ens.}(t) = \sum_{N=0}^{\infty} p_Y(N, t)S_{fix.ens.}(t|N)
- \sum_{N=0}^{\infty} p_Y(N, t) \ln p_Y(N, t).
\]

with

\[
S_{fix.ens.}(t|N) = -\sum_{m=0}^{\infty} p_X(m, t|N) \ln p_X(m, t|N).
\]
A similar line of derivation as above gives:

$$\sum_{N=0}^{\infty} p_Y(N,t)S_{fix.ens}(t|N) = S_{fix.ens}(t|N^*(t)).$$

Therefore, $S_{flu.ens}(t)$ and $S_{fix.ens}(t|N^*(t))$ are related by

$$S_{flu.ens}(t) = S_{fix.ens}(t|N^*(t)) + S_Y(t),$$

(16)

where

$$S_Y(t) = -\sum_{N=0}^{\infty} p_Y(N,t) \ln p_Y(N,t).$$

The first term in the rhs of Eq. (16) corresponds to the entropy associated to the distribution of the $N^*$ fixed particles among the $M$ available states, while the second term corresponds to the entropy associated to variations in the total particle count.

If the peak region of $p_Y(N,t)$ can be approximated by a Poisson distribution, then one can obtain an explicit $S_Y(t) \simeq \frac{1}{2} \ln[2\pi e N^*(t)]$ for large $N^*$ values [36]. In the Appendix B, it is shown that for some examples, $S_{fix.ens}$ can be on the order of $\ln N^*(t)$ as well.

Let us now calculate the time derivative:

$$\frac{dS_{flu.ens}}{dt} = \left(\frac{\partial S_{fix.ens}(t|N^*)}{\partial t}\right)_{N^*} + \left(\frac{\partial S_{fix.ens}(t|N^*)}{\partial N^*}\right)_t \frac{dN^*(t)}{dt} + \frac{dS_Y(t)}{dt}.$$  

(17)

The additional terms in the entropy change are interpreted as follows: For a fixed ensemble, $N^*$ is simply a system constant and $s = (\partial S_{fix.ens}/\partial N^*)_t$ is the entropy change of the system due to the fluctuating ensemble. In Gibbs’ theory, $s$ is called the partial molar entropy. The last term in (17) is, of course, the entropy change associated with fluctuations in total particle count.

Comparing Eq. (17) and Eq. (13), we see that the extra terms in entropy change have to precisely compensate the term with extra terms in energy change so that no extra term appears in Eq. (13). This is the essential idea of the entropy-enthalpy compensation [19, 20].

IV. MICROCANONICAL, CANONICAL AND GRAND CANONICAL MARKOV SYSTEMS

We now apply the above general mathematical results to several special cases.
Canonical and grand-canonical Markov systems. Consider two Markov systems, one with a fixed number of identical, independent particles and one with a variable number of particles due to “birth” and “death” processes. The latter, a grand-canonical Markov system (gcMS), was introduced in [28, 29]. As an ideal gas, a gcMS consists of identical, independent particles each with $M$ possible states. The state of a gcMS is thus represented by \( \{ n_k \mid 1 \leq k \leq M \} \). The total number of particles in the system, \( \sum_{k=1}^{M} n_k = N \), fluctuates. There are two types of “kinetic cycles” in a gcMS. The first type, which also occurs in a canonical Markov system (cMS), involves state transitions of particles without changing the total number of particles, as shown in Fig. 1A. The second type, which only occurs in gcMS, involves adding and removing a particle, as shown in Fig. 1B.

\[
\begin{align*}
(\ldots, n_k, \ldots, n_\ell, \ldots, n_h, \ldots) & \xrightarrow{\frac{n_k q_{k\ell}}{(n_\ell + 1) q_{\ell k}}} (\ldots, n_k - 1, \ldots, n_\ell + 1, \ldots, n_h, \ldots) \\
(n_h + 1) q_{hk} & \xrightarrow{n_k q_{kh}} (n_\ell + 1) q_{th} \xrightarrow{(n_h + 1) q_{hl}} (\ldots, n_k - 1, \ldots, n_\ell, \ldots, n_h + 1, \ldots)
\end{align*}
\]

(A)

\[
\begin{align*}
(\ldots, n_k - 1, \ldots, n_\ell, \ldots) & \xrightarrow{\nu_k} (\ldots, n_k, \ldots, n_\ell, \ldots) \\
(n_\ell + 1) \eta_\ell & \xrightarrow{\nu_\ell} (n_k q_{k\ell}) \xrightarrow{(n_\ell + 1) q_{\ell k}} (\ldots, n_k - 1, \ldots, n_\ell + 1, \ldots)
\end{align*}
\]

(B)

FIG. 1: In a grand-canonical Markov system (gcMS), there are two types of kinetic cycles: (A) state transitions of particles without changing the total number of particles; and (B) cycles involving addition and removal of particles. For gcMS with detailed balance, one has $q_{k\ell} q_{\ell h} q_{hk} = q_{\ell k} q_{h\ell} q_{kh}$ and $\nu_k q_{k\ell} \eta_\ell = \eta_k q_{\ell k} \nu_\ell$ for each cycle type, respectively.

We shall limit our discussions only to non-driven systems. The detailed balance conditions are $q_{k\ell} q_{\ell h} q_{hk} = q_{\ell k} q_{h\ell} q_{kh}$, for the cycle in Fig. 1A, and $\nu_k q_{k\ell} \eta_\ell = \nu_\ell q_{\ell k} \eta_k$, for the cycle in Fig. 1B. With detailed balance, the stationary distribution for the Markov system is easy to obtain. The first cycle type dictates a stationary distribution \( \{ p^*_i \mid 1 \leq i \leq M \} \) for a single particle independent of $N$, such that $p^*_i q_{ij} = p^*_j q_{ji}$. Then the conditional probability
distribution is given by

\[ p^{eq}(n_1, \cdots, n_M|N) = \frac{N!}{n_1! \cdots n_M!} (p_1^*)^{n_1} \cdots (p_M^*)^{n_M}. \] (18)

The detailed balance for the second type of cycles yields \( \nu_k / (\eta_k p_k^*) = \nu_\ell / (\eta_\ell p_\ell^*) = \lambda \), which is a constant, and

\[ p^{eq}(n_1, \cdots, n_M|N) P_N^\text{eq}(N) n_k \eta_k = p^{eq}(n_1, \cdots, n_k - 1, \cdots, n_M|N - 1) P_N^\text{eq}(N - 1) \nu_k. \]

That is,

\[ \frac{p_N^{eq}(N)}{p_N^{eq}(N - 1)} = \frac{\nu_k}{\eta_k N p_k^*} = \frac{\lambda}{N}. \] (19)

This yields a Poisson distribution with mean \( \lambda \), the equilibrium mean particle count in the system. The same result obtained from the grand-canonical ensemble theory with \( \ln \lambda \) being the chemical potential. Thus, the equilibrium distribution for fluctuating \( N \) is

\[ p^{eq}(n_1, \cdots, n_M) = e^{-\lambda} \prod_{\ell=1}^M \frac{(p_\ell^* \lambda)^{n_\ell}}{n_\ell!}. \] (20)

From Eq. (18), one has the following nonequilibrium stochastic free energy for an arbitrary distribution \( p(\{n_k\}|N) \) with fixed \( N \) in a canonical Markov system (cMS) [1]:

\[ F_{cMS}(t|N) = \sum_{n_1, \cdots, n_M|N} p(n_1, \cdots, n_M|N) \ln \left( \frac{p(n_1, \cdots, n_M|N)}{p^{eq}(n_1, \cdots, n_M|N)} \right) \]

\[ = \sum_{k=1}^M \langle n_k \rangle (- \ln p_k^*) - S_N + \sum_{n_1, \cdots, n_M|N} p(\{n_k\}|N) \ln \left( \frac{n_1! \cdots n_M!}{N!} \right), \] (21)

in which the first term is the mean internal energy, the second term is the entropy \( S_N = - \sum p(\{n_k\}|N) \ln p(\{n_k\}|N) \), and the third term is the “entropy of mixing”.

From Eq. (20) one finds that the non-equilibrium stochastic free energy for the gcMS with fluctuating \( N \), mean \( N^*(t) \), and equilibrium mean \( \lambda \), is:

\[ F_{gcMS}(t) = - \sum_{k=1}^M \langle n_k \rangle \ln p_k^* - \tilde{S} + \sum_{n_1, \cdots, n_M} p(\{n_k\}) \ln \left( \frac{n_1! \cdots n_M!}{e^{-\lambda} N^{n_1 + \cdots + n_M}} \right). \] (22)

In the large number limit, the difference between \( S_N \) and \( \tilde{S} = - \sum p(\{n_k\}) \ln p(\{n_k\}) \) is of the order of \( (\ln \langle N \rangle)/2 \), which can be neglected. Regarding the third terms in Eqs. (21) and (22), we show in Appendix C that in the thermodynamic limit, they differ by \( N^*(t)(\ln N^*(t) - \ln \lambda) - (N^*(t) - \lambda) \). This is precisely the \( V \phi(z) \) expected from Eq. (18), with \( \phi(z) = z \ln(z/\overline{z}) - (z - \overline{z}) \), \( z = N^*(t)/V \), and \( \overline{z} = \lambda/V \) (see also Appendix D).
In analogy with classical statistical mechanics, $F_{cMS}$ and $F_{gcMS}$ respectively correspond to the Helmholtz free energy and to negative $pV$. Therefore, their difference is a generalization of Gibbs’ free energy:

$$G(t) = F_{gcMS}(t) - F_{cMS}(t|N^*(t))$$

$$= N^*(t) \ln \left( \frac{N^*(t)}{\lambda} \right) - (N^*(t) - \lambda). \quad (23)$$

It is not hard to prove from (23) that $G \geq 0$ and that $G = 0$ if and only if $N^* = \lambda$. Moreover,

$$\frac{dG}{dt} = \frac{dG}{dN^*} \frac{dN^*}{dt} = \frac{dN^*}{dt} \times \ln \frac{N^*(t)}{\lambda}. \quad (24)$$

Thus, we can see $G(N)$ as a potential and $dG/dN = \ln(N/\lambda)$ as the corresponding chemical force, whereas the rate of change of $G$ is given as the product of the force and the corresponding chemical flux $dN/dt$. The $-N^*$ term in (23) has repeatedly appeared in chemical kinetic literature for systems without conservation of total particle numbers [37].

Eq. (24) therefore provide a justification for the thermodynamic formalism based on the theory of stochastic free energy.

Finally, recall that $F_{cMS}(t)$ measures the Kullback-Leibler divergence between the current probability distribution $p(n_k|N^*(t))$, and the corresponding stationary probability distribution, $p^{eq}(n_k|N^*(t))$. Now, if we assume a separation of time scales such that the distribution $p(n_k|N^*(t))$ rapidly converges to $p^{eq}(n_k|N^*(t))$, as compared with $p(N,t)$, then $F_{gcMS}(t) \approx 0$ and

$$G(t) = F_{gcMS}(t).$$

**Canonical and microcanonical Markov systems.** We now consider a Markov system with joint stationary distribution for $X$ and $Y$, with stationary $p_{XY}^{ss}(x,y) = p_{X|Y=y}^{ss}(x)P_Y^{ss}(y)$. Let us further assume that the conditional probability $p_{X|Y=y}^{ss}(x)$ is uniform, i.e. a microcanonical ensemble:

$$p_{X|Y=y}^{ss}(x) = \frac{1}{\Omega_y}. \quad (25)$$

Then, by applying the general formalism in Sec. III we have

$$F_{XY}(t) = \sum_y P_Y(y)F_{X|Y=y}(t) + \sum_y P_Y(y) \ln \left( \frac{P_Y(y)}{P_Y^{ss}(y)} \right), \quad (26)$$

with

$$F_{X|Y=y} = \ln \Omega_y + \sum_x p_{X|Y=y}(x) \ln p_{X|Y=y}(x) = \ln \Omega_y - S_{X|Y=y}. \quad (27)$$
Furthermore, in the thermodynamic limit:

$$\sum_y P_Y(y) \ln \left( \frac{P_Y(y)}{P_{ss}^Y(y)} \right) = -\ln P_{ss}^Y(y^*(t)), \quad (28)$$

where $y^*(t) = \sum_y y P_Y(y)$. Therefore,

$$F_{XY}(t) = -S_{X|Y=y^*}(t) + \ln \Omega_{y^*}(t) - \ln P_{ss}^Y(y^*(t)) = -S_{X|Y=y^*}(t) + E(y^*(t)). \quad (29)$$

The steady-state “internal energy” $E(y)$ thus satisfies $P_{ss}^Y(y) = \Omega_y e^{-E(y)}$, which one can clearly recognize from the canonical ensemble theory in classical statistical mechanics ($k_B T = 1$)—these results are in agreement with a theorem by van Campenhout and Cover [38, 39].

In conclusion, we can see that the stochastic free energy approach provides yet another interpretation for the mathematics, complementary to that of Boltzmann or E.T. Jaynes [39].

V. SUMMARY

In summary, in the thermodynamic limit with an infinite system size, the chain rule for relative entropies yields a Legendre transform for the stochastic free energy: $F_{flu.ens}(t) = F_{fix.ens}(t|y^*) - \ln P_{ss}^Y(y^*)$. In this relation, $\ln P_{ss}^Y(y) = -V \phi(y/V) = N \mu$, with $V$ representing the system size, while $\mu = -(V/y) \phi(y/V)$ is the thermodynamic conjugate variable for the random variable $Y$.

The time evolutions $(d/dt)F_{flu.ens}(t) = (\partial/\partial t)F_{fix.ens}(t|y^*)$. However, for the entropy we have that $(d/dt)S_{flu.ens}(t) = (\partial/\partial t)S_{fix.ens}(t|y^*(t)) + s(t)(d/dt)y^*(t) + (d/dt)S_Y$, where $s(t) = (\partial/\partial y^*)S_{fix.ens}(t|y^*(t))$ is the partial molar entropy.

The general theory of nonequilibrium stochastic free energy and ensemble change, associated with the conditional probability, can be applied to systems of fixed and variable numbers of identical random variables. For instance, the canonical and grand canonical systems. In this case we obtain $F_{flu.ens}(t) = F_{fix.ens}(t) + N^*(t)(\ln N^*(t) - \ln \lambda) - (N^*(t) - \lambda)$, $\lambda$ being the equilibrium mean particle count of the system. The difference between $F_{flu.ens}(t)$ and $F_{fix.ens}(t)$, which respectively correspond to the $-pV$ and the Helmholtz free energy in classical thermodynamics, can then be interpreted as the Gibbs free energy: the “chemical” work performed upon the system to change its particle count.
When we consider a Markov system with joint stationary $X$ and $Y$, and a uniform conditional distribution $p_{X|Y=y}^s = \Omega_y^{-1}$, we obtain $F_{XY}(t) = -S_{X|Y=y^*}(t) + E(y^*)(t)$, where $S_{X|Y=y^*}$ is the entropy of the microcanonical system, and the “internal energy” satisfies $P_{Y}^{s*}(y) = \Omega_y e^{-E(y)}$. This example suggests a rather novel interpretation for Gibbs’ canonical ensemble theory. From a stochastic Markov dynamics perspective, entropy and free energy are inherent concepts associated with a system’s dynamics [1], while the internal energy is an emergent concept for a canonical ensemble with a underlying microcanonical structure: $E(y) = \ln(\Omega_y/P_{Y}^{s*}(y))$ where $\Omega_y$ is Boltzmann’s thermodynamic probability. This interpretation of the internal energy as an emergent concept is in sharp contrast to the logic usually presented in textbooks where it is given a priori based upon Newtonian mechanics. This view, however, is in agreement with [13], in which a thermodynamic formalism based on free energy for “Darwinian dynamics” has been proposed. It was suggested that the canonic ensemble, i.e. Boltzmann-Gibbs type of distribution, is a natural consequence of Darwinian dynamics.

The internal energy defined as above, $E(y)$, is a function of the random variable. It is a fluctuating quantity. Its physical origin can lie outside the system, due to the interactions between the system and its environment. This should not be a surprise since in classical mechanics, potential energy can also be due to external forces, e.g. gravitation.

VI. ACKNOWLEDGEMENT

We thank Drs. M.J. de Oliveira, Massimiliano Esposito, Hao Ge, Michael Mackey and Hugo Touchette for helpful comments.
[1] H. Ge and H. Qian (2010) Phys. Rev. E. 81, 051133.
[2] M. Esposito and C. van den Broeck (2010) Phys. Rev. Lett. 104, 090601.
[3] H. Ge (2009) Phys. Rev. E. 80, 021137.
[4] M. Esposito, U. Harbola and S. Mukamel (2007) Phys. Rev. E. 76, 031132.
[5] C. Jarzynski (2011) Annu. Rev. Cond. Matt. Phys. 2, 329–251.
[6] G. Nicolis and I. Prigogine (1977) *Self-Organization in Nonequilibrium Systems*, Wiley-Interscience, New York.
[7] D.-Q. Jiang, M. Qian and M.-P. Qian (2004) *Mathematical Theory of Nonequilibrium Steady States*, LNM vol. 1833, Springer-Verlag, Berlin.
[8] X.-J. Zhang, H. Qian and M. Qian (2012) Phys. Rep. 510, 1–86.
[9] H. Ge, M. Qian and H. Qian (2012) Phys. Rep. 510, 87–118.
[10] J. Voigt (1981) Comm. Math. Phys. 81, 31–38.
[11] T.M. Cover and J.A. Thomas (2006) *Elements of Information Theory*, 2nd ed., Wiley-Interscience, New York.
[12] M.C. Mackey (1989) Rev. Mod. Phys. 61, 981–1015.
[13] P. Ao (2008) Comm. Theor. Phys. 49, 1073–1090.
[14] M. Santillán and H. Qian (2011) Phys. Rev. E. 83, 041130.
[15] M. Esposito (2011) arXiv:1112.5410.
[16] J. G. Kirkwood (1935) J. Chem. Phys. 3, 300–313.
[17] T.L. Hill (1987) *Statistical Mechanics: Principles and Selected Applications*, Dover, New York.
[18] G. Gallavotti (1999) *Statistical Mechanics: A Short Treatise*, Springer, New York.
[19] H. Qian and J.J. Hopfield (1996) J. Chem. Phys. 105, 9292–9296.
[20] H. Qian (1998) J. Chem. Phys. 109, 10015–10017.
[21] T.L. Hill (2001) Nano Lett. 1, 273–275.
[22] T.L. Hill (1994) *Thermodynamics of Small Systems*, Dover: New York.
[23] H. Qian (2012) J. Biol. Phys. (Springer) to appear.
[24] H. Qian (2002) Phys. Rev. E. 65, 016102.
[25] R.K.P. Zia, E.F. Redish and S.R. McKay (2009) Am. J. Phys. 77, 614–622.
[26] M. J. de Oliveira (2003) Phys. Rev. E. 67, 027104.
[27] M. J. de Oliveira and T. Tomé (2008) Eur. Phys. J. B 64, 409–414.
[28] W.J. Heuett and H. Qian (2006) J. Chem. Phys. 124, 044110.
[29] C. Gadgil, C.H. Lee and H.G. Othmer (2005) Bull. Math. Biol. 67, 901–946.
[30] E. S. Zeron and M. Santillán (2011) Meth. Enzymol. 487C, 149-171.
[31] H. Touchette (2009) Phys. Rep. 478, 1–69.
[32] H. Touchette and R.J. Harris (2011) arXiv:1110.5216v1.
[33] H. Ge and H. Qian (2011) J. R. Soc. Interf. 8, 107–116.
[34] M. Vellela and H. Qian (2009) J. R. Soc. Interf. 6, 925–940.
[35] R.H. Fowler (1967) Statistical Mechanics, 2nd ed., Cambridge Univ. Press, U.K.
[36] R.J. Evans and J. Boersma (1988) SIAM Rev. 30, 314–317.
[37] H. Qian and D.A. Beard (2005) Biophys. Chem. 114, 213–220.
[38] J.M. van Campenhout and T.M. Cover (1981) IEEE Trans. Info. Th. 27, 483–489.
[39] H. Ge and H. Qian (2011) arXiv:1105.4118.
Appendix A: Kullback-Leibler divergence of Poisson distributions

A Poisson distribution has the probability mass function (pmf):

\[ P_\lambda(k) = \frac{\lambda^k}{k!} \exp(-\lambda), \tag{A1} \]

were \( \lambda \) is the corresponding mean value. It follows that

\[ \sum_{k=0}^{\infty} P_{\lambda_1}(k) \ln \left( \frac{P_{\lambda_1}(k)}{P_{\lambda_2}(k)} \right) = \lambda_1 \ln \left( \frac{\lambda_1}{\lambda_2} \right) - (\lambda_1 - \lambda_2). \tag{A2} \]

On the other hand, under the assumption that \( \lambda_1 \gg 1 \) and Stirling’s formula \( \ln(\lambda_1!) \simeq \lambda_1 \ln \lambda_1 - \lambda_1 \), we have

\[ \ln (P_{\lambda_2}(\lambda_1)) \simeq -\lambda_1 \ln \left( \frac{\lambda_1}{\lambda_2} \right) + (\lambda_1 - \lambda_2). \tag{A3} \]

We therefore obtain that

\[ \sum_{k=0}^{\infty} P_{\lambda_1}(k) \ln \left( \frac{P_{\lambda_1}(k)}{P_{\lambda_2}(k)} \right) \simeq -\ln (P_{\lambda_2}(\lambda_1)). \tag{A4} \]

Appendix B: Entropy for a system of \( N \) particles distributed in \( M \) different states

We give an example that \( S_{\text{fix.ens}} \) is on the order of \( \ln N \). Again, considering total \( N \) identical, independent particles, each with \( M \) possible states. Let \( m_i \) be the occupation numbers for the state \( i \), \( \sum_{i=1}^{M} m_i = N \). It is straightforward to demonstrate by induction that, given \( N \) and \( M \), the number of possible, different occupation-number sets \( \{m_i\} \) is given by

\[ \frac{(N + M - 1)!}{N!(M - 1)!}. \tag{B1} \]

The maximum possible entropy occurs when every occupation-number set has the same probability. Therefore, it is given by

\[ S_{\text{max}} = \ln \frac{(N + M - 1)!}{N!(M - 1)!}. \tag{B2} \]

In the limit when \( N \gg M \), \( (N + M - 1)!/N! \simeq N^{M-1} \), and so

\[ S_{\text{max}} \simeq (M - 1) \ln N - \ln(M - 1)! \simeq (M - 1) \ln N. \tag{B3} \]
Appendix C: Entropy of mixing for the grand canonical and canonical Markov systems

Consider the term
\[ \Gamma_{gcMS} = \sum_{n_1, \ldots, n_M} p(\{n_k\}) \ln \left( \frac{n_1! \cdots n_M!}{e^{-\lambda n_1 + \cdots + n_M}} \right). \]

By making use of the conditional probability it can be rewritten as
\[ \Gamma_{gcMS} = \sum_{N} p(N) \sum_{n_1, \ldots, n_M|N} p(\{n_k\}|N) \ln \left( \frac{n_1! \cdots n_M!}{N!} \right) - \sum_{N} p(N) \ln \left( \frac{e^{-\lambda N}}{N!} \right). \quad (C1) \]

Noting that the Poisson distribution \( P_\lambda(N) \) satisfies
\[ -\ln(P_\lambda(N)) = -\ln \left( \frac{e^{-\lambda N}}{N!} \right) \simeq N \ln \left( \frac{N}{\lambda} \right) - (N - \lambda), \]
when \( N \gg 1 \), \( \Gamma_{gcMS} \) can be approximated by
\[ \Gamma_{gcMS} \simeq \Gamma_{cMS} + N^* \ln \left( \frac{N^*}{\lambda} \right) + (N^* - \lambda), \quad (C2) \]
with \( N^* = \sum_{N} N p(N) \) and
\[ \Gamma_{cMS} = \sum_{n_1, \ldots, n_M|N^*} p(\{n_k\}|N^*) \ln \left( \frac{n_1! \cdots n_M!}{N^*!} \right). \quad (C3) \]

Appendix D: Asymptotic approximation of a Poisson distribution for large \( N \)

For the Poisson distribution
\[ P_\lambda(N) = \frac{\lambda^N e^{-\lambda}}{N!}, \]
when \( N \gg 1 \), one can approximate
\[ P_\lambda(N) \simeq \frac{\lambda^N e^{-\lambda}}{N^N e^{-N}}. \]

Therefore,
\[ -\ln(P_\lambda(N)) \simeq N \ln \left( \frac{N}{\lambda} \right) - (N - \lambda), \quad (D1) \]
or,
\[ \phi(z) = -\frac{1}{V} \ln(P_\lambda(N)) \simeq z \ln \left( \frac{z}{\lambda} \right) - z + \text{const.}, \quad (D2) \]
in which \( z = N/V \) is the number density and \( \overline{z} = \lambda/V \) is the mean number density. Eq. (D1) is valid for large \( N \) with both large and small \( \lambda \). The form given in (D2) has been known as the macroscopic free energy functional for a closed chemical reaction systems with mass-action kinetics [37]. This is consistent with the fact that for a closed chemical kinetic system a multi-Poisson representation exists for its equilibrium distribution according to the Delbrück-Gillespie theory [34].