GALLAVOTTI–COHEN–TYPE SYMMETRY RELATED TO CYCLE DECOMPOSITIONS FOR MARKOV CHAINS AND BIOCHEMICAL APPLICATIONS

ALESSANDRA FAGGIONATO AND DANIELE DI PIETRO

ABSTRACT. We slightly extend the fluctuation theorem obtained in [24] for sums of generators, considering continuous–time Markov chains on a finite state space whose underlying graph has multiple edges and no loop. This extended frame is suited when analyzing chemical systems. As simple corollary we derive by a different method the fluctuation theorem of D. Andrieux and P. Gaspard for the fluxes along the chords associated to a fundamental set of oriented cycles [3].

We associate to each random trajectory an oriented cycle on the graph and we decompose it in terms of a basis of oriented cycles. We prove a fluctuation theorem for the coefficients in this decomposition. The resulting fluctuation theorem involves the cycle affinities, which in many real systems correspond to the macroscopic forces. In addition, the above decomposition is useful when analyzing the large deviations of additive functionals of the Markov chain. As example of application, in a very general context we derive a fluctuation relation for the mechanical and chemical currents of a molecular motor moving along a periodic filament.

Keywords: nonequilibrium steady state, thermodynamic force, affinity, large deviation, generating function, oriented cycle, spanning tree, fluctuation theorem, molecular motor.

1. Introduction

Out–of–equilibrium systems are common in daily life. Examples are mechanical systems in contact with thermal reservoirs as well reacting systems in contact with particle reservoirs generating particle fluxes through differences of chemical potentials. Considering chaotic dynamical systems of statistical mechanics, Gallavotti and Cohen [10] have discovered a symmetry relation (now taking their names) for the large deviation functional of the average entropy creation rate. This relation is also called fluctuation theorem. The same result has then been derived for Markov stochastic processes by Kurchan [19], Maes [25] and Lebowitz and Spohn [24]. An extensive rigorous treatment including further developments is given in the book of Jiang et al. [15] (see also references therein together with [6]). Near to equilibrium, the fluctuation theorem generalized to systems with several currents yields the Onsager’s symmetry and the usual Green–Kubo’s formulas for transport coefficients [11] [24]. In this sense, it can be thought as their generalization far from equilibrium.

Work partially supported by the European Research Council through the “Advanced Grant” PTRELSS 228032.
The initial investigation of the fluctuation theorem has referred to models coming from statistical mechanics, and in the last years a proper analysis has been developed for chemical and biochemical systems by Andrieux and Gaspard (see for example [12][1][2][3][4][5] and references therein). The analysis for a model of molecular motor along a periodic filament with two chemical states has also been done by Lacoste, Lau, Mallick [20][21][22][23].

The approach of Andrieux and Gaspard is much inspired by the network theory of out–of–equilibrium systems. This theory has been developed by Hill [13] and Schnakenberg [30] with a special attention to biochemical systems. Mathematically, one is interested to the stochastic dynamics of a continuous time random walk on a finite connected graph $\mathcal{G}$ with multiple edges and no loop, where the jumps along an edge have positive probability rate in both directions. For such a random walk the stationary distribution $\mu$ exists and is unique. To each oriented bond $\ell$ in $\mathcal{G}$ from the state $\sigma$ to the state $\sigma'$, one associates a microscopic affinity defined as

$$A(\ell) = \ln \frac{\mu(\sigma)k(\sigma,\sigma')}{\mu(\sigma')k(\sigma',\sigma)},$$

(1.1)

where $k(\sigma_1,\sigma_2)$ denotes the probability rate for a jump from $\sigma_1$ to $\sigma_2$. Note that detailed balance in reversible systems simply corresponds to the fact that all microscopic affinities are zero. The affinity associated to a given oriented cycle $\mathcal{C}$ in $\mathcal{G}$ is then defined as the sum of the microscopic affinities of the oriented bonds forming the cycle: $A(\mathcal{C}) = \sum_{\ell \in C} A(\ell)$. It is simple to check that the affinity of a cycle remains the same if one replaces the above microscopic affinity $A(\ell)$ by $\ln(k(\sigma,\sigma')/k(\sigma',\sigma))$.

The network theory presented in [30] is based on the fact that to each unoriented spanning (maximal) tree on the graph $\mathcal{G}$ one can associate in a canonical way a family of oriented cycles, called fundamental set of oriented cycles, being a sort of basis of the space of all oriented cycles. Each oriented cycle in a fundamental set contains only one oriented edge (called chord) that does not belong to the spanning tree when disregarding orientation. In [30] Schnakenberg has observed that, for several models of real systems, the macroscopic (mechanical or thermodynamical) forces keeping the system out–of–equilibrium are the affinities of the oriented cycles of some fundamental set in $\mathcal{G}$ (note that more oriented cycles can have the same affinity). In [3] this situation is called Schnakenberg condition. We point out (see [30][3]) that usually thermodynamic forces are not encoded in a single jump rate.

In [3], starting from a spanning tree, Andrieux and Gaspard have derived a fluctuation theorem for the currents along the chords, whose conjugate variables are the affinities associated to the oriented cycles in the fundamental set. Under the Schnakenberg condition, this fluctuation theorem can be restated in terms of the macroscopic forces keeping the system out–of–equilibrium instead of cycle affinities.

Let us explain our theoretical contribution in this direction. First, we recover the above results of Andrieux and Gaspard by a different approach. Indeed, the fluctuation theorem presented for sums of several generators in Section 2.3 of [24] is not suited for random walks on graphs with multiple edges, but as we show its simple proof can be easily adapted to the present case. This slightly extended result immediately leads to the fluctuation theorem for the family of currents along all
oriented edges, and therefore to the fluctuation theorem for the currents referred to a fundamental set of oriented cycles. We point out that the fundamental sets of oriented cycles, canonically associated to the spanning trees of the graph $G$, do not cover all possible bases of the cycle space. We then extend the network theory presented in [30] and prove a fluctuation theorem for the “currents” referred to a generic basis of oriented cycles. When dealing with a generic basis, chords disappear and the definition of the variables conjugated to the affinities of the oriented cycles in the basis is more algebraic. We call these conjugate variables generalized currents. Their definition needs to associate to each random trajectory an oriented cycle, which must then be decomposed in the basis. The generalized currents are the coefficients in this decomposition. Their definition is essentially algebraic and differs from the derived chain discussed in [15] (Chapters 1, 2). In the derived chain method, for each oriented cycle $C$ one counts the number of times $\omega_t(C)$ that the cycle has been realized by the trajectory up to a given time $t$ (there is nothing algebraic): in [15] the authors show that this quantity, rescaled by $t$, converges a.s. to some circulation number $\omega(C)$ and show that the entropy production rate in the steady state can be expressed in terms of the circulation numbers. For a discussion on fluctuation theorems satisfied by $\omega_t(C)$ we refer to [5].

The above cycle decomposition of the trajectory is particularly useful when looking for a fluctuation theorem of additive functionals of the Markov chain. As example of application in this direction, we consider a very general discrete model for a molecular motor moving along a periodic filament under the action of an external force $f$, transforming the chemical energy from ATP hydrolysis to mechanical work. The forces keeping the system out–of–equilibrium are the external force $f$ and the chemical potential difference $\Delta \mu$ associated to ATP hydrolysis. In the last years, much attention have been devoted to the thermodynamics of small systems supported by very fast technological improvements (see for example [8, 29] and references therein). Molecular motors are proteins working as motors at the nanoscale, with very interesting thermodynamic aspects, which have been much investigated both from a theoretical and an experimental viewpoint [14, 16, 17, 28]. The fluctuation theorem for molecular motors with two or three chemical states have been proved in [1] and [20, 21, 22, 23]. The small number of chemical states allows a detailed analysis based on matrix computations, leading to more information than the Gallavotti–Cohen–type symmetry for large deviations. In the general case, matrix computations become not reasonable. On the other hand, the developed theory for fluctuation theorems associated to cycle decompositions allows to easily prove in full generality the fluctuation relation obtained in [21, 22] for only two chemical states. More precisely, calling $x_t$ the position of the molecular motor along the filament and $z_t$ the ATP consumption, it holds

$$\vartheta(\lambda, \gamma) = \vartheta(f \beta - \lambda, \beta \Delta \mu - \gamma), \quad \lambda, \gamma \in \mathbb{R}, \quad (1.2)$$

where, roughly speaking, the function $\vartheta(\lambda, \gamma)$ is characterized by the identity

$$e^{-\vartheta(\lambda, \gamma)t} \sim \mathbb{E}(e^{-\lambda x_t - \gamma z_t}), \quad t \gg 1, \quad (1.3)$$
and where $\overrightarrow{\beta}$ and $\bar{x}_i$ denote the dimensionless quantities $f\beta \times [1m]$ and $x_i/[1m]$ ([$1m$] being the length unit). Of course, $\beta = 1/kT$ where $k$ is the Boltzmann’s constant and $T$ the absolute temperature.

1.1. Outline of the paper. In Section 2 we extend the fluctuation theorem for sums of generators (see Theorem 2.1). In Section 3 we discuss some fluctuation theorems (Fact 3.3 and Theorem 3.5) related to cycle decompositions (fundamental set of oriented cycles and basis, respectively). All proofs are postponed to Sections 4.5 and 6. Finally, in Section 4 we discuss the biochemical application of Theorem 3.5 leading to relation (1.2).

2. Fluctuation Theorem for sums of Markov generators

As starting point, we extend the fluctuation theorem obtained in [24] [Section 2.3]. As in [24] we consider a continuous–time Markov chain $(X_t)_{t \geq 0}$ on a finite state space $\mathcal{S}$ having Markov generator

$$\mathcal{L} f(\sigma) = \sum_{\sigma' : \sigma' \neq \sigma} k(\sigma, \sigma')(f(\sigma') - f(\sigma)), \quad \sigma \in \mathcal{S}. \quad (2.1)$$

We assume that the Markov chain is irreducible and that the transition rates satisfy the positivity relation

$$k(\sigma, \sigma') > 0 \iff k(\sigma', \sigma) > 0. \quad (2.2)$$

The last assumption is very reasonable in physical systems, since for a real transition between physical states one expects that, at least with very low probability, the opposite transition is possible. We remark that, due to irreducibility and since $\mathcal{S}$ is finite, there exists a unique stationary distribution of the Markov chain.

We decompose the generator $\mathcal{L}$ as a sum of $m$ generators $\mathcal{L}^{(i)}$. More precisely, we fix a family of numbers $k^{(i)}(\sigma, \sigma')$, parameterized by the index $i = 1, \ldots, m$ and by the pairs $(\sigma, \sigma')$ of distinct elements in $\mathcal{S}$. We assume that:

(A1) $k^{(i)}(\sigma, \sigma') \geq 0$ for all $i : 1 \leq i \leq m$ and $\sigma \neq \sigma'$ in $\mathcal{S}$;

(A2) $\sum_{i=1}^{m} k^{(i)}(\sigma, \sigma') = k(\sigma, \sigma')$ for all $\sigma \neq \sigma'$ in $\mathcal{S}$;

(A3) $k^{(i)}(\sigma, \sigma') > 0 \iff k^{(i)}(\sigma', \sigma) > 0$, for all $i : 1 \leq i \leq m$ and $\sigma \neq \sigma'$ in $\mathcal{S}$.

Trivially, the above family $\{k^{(i)}(\sigma, \sigma')\}_{i,\sigma,\sigma'}$ corresponds to a representation of $\mathcal{L}$ as sum of Markov generators, since we can write $\mathcal{L} = \sum_{i=1}^{m} \mathcal{L}^{(i)}$ where $\mathcal{L}^{(i)}$ denotes the Markov generator on $\mathcal{S}$ defined as $\mathcal{L}^{(i)} f(\sigma) = \sum_{\sigma', \sigma' \neq \sigma} k^{(i)}(\sigma, \sigma')(f(\sigma') - f(\sigma)).$

We point out that our assumptions (A1), (A2), (A3) coincide with the ones stated in [24] [Section 2.3], with the only exception that here we have dropped the additional assumption of [24] that, given $\sigma \neq \sigma'$, there exists at most one index $i$ such that $k^{(i)}(\sigma, \sigma') > 0$.

The above construction suggests to think of the Markov chain as a random walk on a connected graph $\mathcal{G}$ with multiple edges and no loop: the vertexes of $\mathcal{G}$ are given by the states of $\mathcal{S}$, while two distinct states $\sigma, \sigma'$ are linked by as many edges as the indexes $i$ for which $k^{(i)}(\sigma, \sigma'), k^{(i)}(\sigma', \sigma) > 0$, each edge is labeled by the corresponding index $i$. Then, $k^{(i)}(\sigma, \sigma')$ represents the probability rate for a jump.
along the \( i \)-labeled edge from \( \sigma \) to \( \sigma' \). Such an interpretation of the Markov chain as random walk on a graph with multiple edges becomes particularly relevant in biochemical applications and is essential when considering thermodynamical forces and affinities \([13, 30, 12, 3]\).

We formulate the fluctuation theorem in terms of the random walk on the graph \( G \) presented above. By a trajectory up to time \( t \), we mean the path \((X_s : s \in [0, t])\) together with the knowledge of the edges along which the walker has moved. Given \( i : 1 \leq i \leq m \) and states \( \sigma \neq \sigma' \), we define the weight

\[
w^{(i)}(\sigma, \sigma') := \begin{cases} \ln \frac{k^{(i)}(\sigma, \sigma')}{k^{(i)}(\sigma', \sigma)} & \text{if } k^{(i)}(\sigma, \sigma'), k^{(i)}(\sigma', \sigma) > 0; \\ 0 & \text{otherwise}. \end{cases}
\]

(2.3)

To each trajectory up to time \( t \), visiting the states \( \sigma_0, \sigma_1, \ldots, \sigma_n \) (listed in chronological order, \( n \) being a random integer) and jumping along the (unoriented) edges indexed respectively by \( i_0, i_1, \ldots, i_{n-1} \), we associate the functions \( W^{(i)}(t) \), \( i : 1 \leq i \leq m \), defined as

\[
W^{(i)}(t) := \sum_{k=0}^{n-1} w^{(i)}(\sigma_k, \sigma_{k+1}) \delta_{i_k=i}.
\]

(2.4)

 Shortly, every time the walker jumps along an \( i \)-edge, the function \( W^{(i)} \) increases of the weight \( w^{(i)}(\sigma, \sigma') \), \( \sigma \) and \( \sigma' \) being the initial state and the final state of the jump.

In what follows, given a distribution \( \nu \) on \( S \) we denote by \( \mathbb{P}_\nu \) and \( \mathbb{E}_\nu \) the probability measure and the expectation w.r.t. the Markov chain \( X_t \) with knowledge of the crossed edges, starting with initial distribution \( \nu \). If \( \nu = \delta_\sigma \), we simply write \( \mathbb{P}_\sigma \) and \( \mathbb{E}_\sigma \) instead of \( \mathbb{P}_\nu \) and \( \mathbb{E}_\nu \).

We point out that for any \( \lambda_1, \ldots, \lambda_m \in \mathbb{R} \), the moment generating function \( \mathbb{E}_\sigma \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(t)} \right] \) is finite. Indeed, all the weights \( w^{(i)}(\sigma, \sigma') \) are finite, while by a simple coupling argument one gets that the random number of jumps in the time interval \([0, t]\) is stochastically dominated by a suitable Poisson variable, which has finite moment generating function.

Similarly to \([24]\) [Section 2.3] (with the exception that here we consider arbitrarily initial distributions and we have dropped a technical assumption), the following holds:

**Theorem 2.1.** Given a distribution \( \nu \) on \( S \), for each \( \lambda_1, \ldots, \lambda_m \in \mathbb{R} \) the limit

\[
e(\lambda_1, \ldots, \lambda_m) := \lim_{t \to \infty} -\frac{1}{t} \ln \mathbb{E}_\nu \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(t)} \right]
\]

(2.5)

exists, is finite and does not depend on \( \nu \). Moreover, the following fluctuation relation is valid:

\[
e(\lambda_1, \ldots, \lambda_m) = e(1-\lambda_1, \ldots, 1-\lambda_m).
\]

(2.6)
The proof is given in Subsection 5.1. Due to the theory of large deviations (cf. [32], Section 1.5 in [15] and references therein), the Legendre–Fenchel transform
\[ I(z_1, \ldots, z_m) := \sup_{\lambda_1, \ldots, \lambda_m \in \mathbb{R}} \left\{ e(\lambda_1, \ldots, \lambda_m) - \sum_{i=1}^{m} \lambda_i z_i \right\} \]
is convex, lower–semicontinuous and non–negative. Moreover, it has compact level sets and satisfies \( \inf_{z \in \mathbb{R}^m} I(z) = 0 \). In addition, the random vector \( W^{(i)}(t)/t \) satisfies w.r.t. \( \mathbb{P}_\nu \) a large deviation principle with rate function \( I \) (independent from \( \nu \)). As discussed in [24], the fluctuation relation (2.6) can be restated in terms of the rate function \( I \) as
\[ I(z_1, \ldots, z_m) - I(-z_1, \ldots, -z_m) = -\sum_{i=1}^{m} z_i, \quad \forall z \in \mathbb{R}^m. \] (2.7)

Physical implications of the above relations in the steady state are discussed in [24].

We point out that the above Theorem 2.1 leads to an infinite family of fluctuation relations (2.6), parameterized by the decompositions \( L = \sum_{i=1}^{m} L^{(i)} \). Only some of them refer to relevant physical quantities. Some physically relevant cases are discussed in [24], the fundamental one corresponds to \( m = 1 \), in this case \( W^{(1)} \) is related with the entropy production of the system. As explained in Section 3, by a suitable choice of the decomposition \( L = \sum_{i=1}^{m} L^{(i)} \) one immediately recovers from the above theorem the fluctuation theorems for currents obtained in [3].

3. Fluctuation theorem for currents

The dynamical evolution of several physical and chemical systems is already described by a random walk on a finite graph, with multiple edges and no loop. Here, we can apply Theorem 2.1 to this context, obtaining an equivalent fact which is simply formulated in a different language. Moreover, we re–derive the fluctuation theorem for currents with respect to a fundamental set of oriented cycles obtained in [3] and consider a similar problem when working with more general sets of oriented cycles (Theorem 3.5 below).

We start now with a finite connected unoriented graph \( G \) whose vertexes are given by the states in \( S \). \( G \) can have multiple edges but no loop, i.e. between two distinct vertexes \( \sigma, \sigma' \) there can be several edges, while there is no edge from a state to itself. We denote by \( E_o \) (\( o = \text{oriented} \)) the set of edges of \( G \) with orientation (each edge in \( G \) has two possible orientations and therefore corresponds to two oriented edges in \( E_o \)). Given \( \ell \in E_o \), we denote by \( \hat{\ell} \) the edge obtained from \( \ell \) by inverting its orientation. Moreover, we write \( \ell_i \) and \( \ell_f \) for the states in \( S \) such that \( \ell \) goes from \( \ell_i \) to \( \ell_f \) (initial and final states). It is convenient to assign a canonical orientation to each unoriented edge in \( G \). We denote by \( E_c \) (\( c = \text{canonical} \)) the set of canonically oriented edges of \( G \). Note that each oriented edge in \( G \) is given by \( \ell \) or \( \hat{\ell} \), for some \( \ell \in E_c \).

We fix a family of positive numbers \( \{k(\ell)\}_{\ell \in E_c} \) and consider the continuous time random walk \( X_t \) on \( G \), jumping along the edge \( \ell \) (following the associated orientation)
with probability rate $k(\ell)$. In particular, the Markov generator of $X_t$ is given by
\[
\mathcal{L} f(\sigma) = \sum_{\ell \in \mathcal{E}_o, \sigma = \ell} k(\ell) \left( f(\ell) - f(\sigma) \right). \tag{3.1}
\]

Since $\mathcal{G}$ is a connected graph and since the constants $k(\ell)$ are positive, $X_t$ belongs to the class of Markov chains on $\mathcal{S}$ introduced in Section 2.

To each oriented edge $\ell \in \mathcal{E}_o$, we associate the weight
\[
w(\ell) = \ln k(\ell)/k(\bar{\ell}) \tag{3.2}
\]
and we define $N_\ell(t)$ as the number of times the random walk jumps along $\ell$ minus the number of times the random walk jumps along $\bar{\ell}$, up to time $t$. In words, $N_\ell(t)$ is the flux along the oriented edge $\ell$. Considering the sum decomposition $\mathcal{L} = \sum_{\ell \in \mathcal{E}_o} \mathcal{L}(\ell)$ where $\mathcal{L}(\ell)$ is the Markov generator associated only to the jumps along the oriented edges $\ell$ and $\bar{\ell}$, it is trivial to check that Theorem 2.1 implies the following fact:

**Fact 3.1.** For any initial distribution $\nu$ and for any family $\{\lambda_\ell : \ell \in \mathcal{E}_c\}$ of real numbers, the limit
\[
q(\{\lambda_\ell : \ell \in \mathcal{E}_c\}) := \lim_{t \to \infty} \frac{1}{t} \ln \mathbb{E}_\nu \left[ e^{-\sum_{\ell \in \mathcal{E}_c} \lambda_\ell N_\ell(t)} \right] \tag{3.3}
\]
exists, is finite and does not depend on $\nu$. Moreover, it holds
\[
q(\{\lambda_\ell : \ell \in \mathcal{E}_c\}) = q(\{w(\ell) - \lambda_\ell : \ell \in \mathcal{E}_c\}). \tag{3.4}
\]

We point out that, when $\nu$ is the stationary distribution, the above result equals formula (84) in [3].

### 3.1. Fluctuation theorem for currents w.r.t. a fundamental set of oriented cycles.

We recall here some basic concepts concerning the oriented cycles in a finite graph [13, 30, 7, 30] represents a very concise reference.

An oriented cycle $\mathcal{C}$ in $\mathcal{G}$ can be described by a string of oriented edges $(b_1, \ldots, b_k)$, $b_i \in \mathcal{E}_o$, such that the vertex in which $b_i$ enters equals the vertex from which $b_{i+1}$ exits (with the convention $k + 1 = 1$). We convey that the strings $(b_1, \ldots, b_k)$ and $(b_i, b_{i+1}, \ldots, b_k, b_1, \ldots, b_{i-1})$ identify the same oriented cycle $\mathcal{C}$. When disregarding the orientation of $\mathcal{C}$, we call it simply cycle.

We fix a maximal tree (also called spanning tree) $T$ on $\mathcal{G}$, i.e. $T$ is a unoriented subgraph of $\mathcal{G}$, containing all vertexes of $\mathcal{G}$ and containing no cycle. The edges $\ell \in \mathcal{E}_c$ which do not belong to $T$ when disregarding orientation are called chords of the maximal tree $T$. We enumerate the edges in $\mathcal{E}_c$ as $\ell_1, \ell_2, \ldots, \ell_n$ where $\ell_1, \ldots, \ell_s$ are the chords associated to $T$. In particular, $s$ is the number of chords of $\mathcal{G}$. It is simple to prove that $s$ equals $e - v + 1$, where $e$ is the number of edges of $\mathcal{G}$ and $v$ the number of vertexes. In particular, $s$ does not depend on the choice of the maximal tree and will be referred in what follows as chord number.

When adding to $T$ a chord $\ell_i$ (disregarding its orientation), one obtains a graph containing a unique cycle. We give to this cycle the orientation induced by the chord $\ell_i$ and call $\mathcal{C}_i$ the resulting oriented cycle. The set $\{\mathcal{C}_1, \ldots, \mathcal{C}_s\}$ is called a fundamental set of oriented cycles. We now explain the origin of the name. Given an oriented cycle $\mathcal{C}$ and an oriented edge $\ell \in \mathcal{E}_o$, we denote by $S_\ell(\mathcal{C})$ the number of
times \( \ell \) appears in \( C \) minus the number of times the reversed edge \( \bar{\ell} \) appears in \( C \). Then

\[
C = \sum_{j=1}^{s} S_{\ell_j}(C) C_j. \tag{3.5}
\]

The meaning of the above identity is clarified by the following definition:

**Definition 3.2.** Given oriented cycles \( C_1, \ldots, C_k, C'_1, \ldots, C'_r \) and given real numbers \( a_1, \ldots, a_k, a'_1, \ldots, a'_r \), we set

\[
\sum_{i=1}^{k} a_i C_i = \sum_{j=1}^{r} a'_j C'_j \iff \sum_{i=1}^{k} a_i S_{\ell_i}(C_i) = \sum_{j=1}^{r} a'_j S_{\ell_j}(C'_j) \quad \forall \ell \in E_o. \tag{3.6}
\]

We point out that, given a fundamental set \( \{C_1, \ldots, C_s\} \), the oriented edges appearing in \( C_j \) are all distinct, that \( \ell \) and \( \bar{\ell} \) cannot both appear in \( C_j \) and that, for each chord \( \ell_i \), it holds \( S_{\ell_i}(C_j) = \delta_{i,j} \) for \( 1 \leq i, j \leq s \).

Recall the definition of the weight \((3.2)\). Given a generic oriented cycle \( C \) we define its affinity as \( A(C) = \sum_{\ell} w(\ell) \), where the sum is among the edges \( \ell \) visited by the cycle with the proper orientation. Alternatively, one can set

\[
A(C) = \sum_{\ell \in E_o} S_{\ell}(C) w(\ell). \tag{3.7}
\]

We recall that in the above definition one can replace \( w(\ell) \) by the ratio between the local flux along \( \ell \) and the local flux along \( \bar{\ell} \) w.r.t. the steady state or any other probability measure \( \nu \) on the vertex set, giving positive measure to each state, i.e. \( w(\ell) \) can be replaced by \( \ln \left[ \frac{\nu(\ell_i) k(\ell_i)}{\nu(\ell_f) k(\bar{\ell})} \right] \). This leads to an equivalent definition of cycle affinity.

Recall the definition of the random variable \( N_{\ell}(t) \) given just after \((3.2)\). \( N_{\ell}(t) \) represents the flux along the oriented edge \( \ell \) (its generalized derivative is the current). In \( \Theta \), the authors have proved the following result (which trivially leads to a fluctuation theorem for large deviations), that we state here for a general initial distribution (only steady states are considered in \( \Theta \)):

**Fact 3.3.** For any initial distribution \( \nu \) and for any \( \lambda_1, \ldots, \lambda_s \in \mathbb{R} \), the limit

\[
Q(\lambda_1, \ldots, \lambda_s) := \lim_{t \to \infty} -\frac{1}{t} \ln \mathbb{E}_{\nu} \left[ e^{-\sum_{i=1}^{s} \lambda_i N_{\ell_i}(t)} \right] \tag{3.8}
\]

exists, is finite and does not depend on \( \nu \). Moreover, it holds

\[
Q(\lambda_1, \ldots, \lambda_s) = Q(A(C_1) - \lambda_1, \ldots, A(C_s) - \lambda_s). \tag{3.9}
\]

The above Fact \(3.3\) restricted to the steady state corresponds to formula (39) in \( \Theta \). As observed there, under Schnakenberg’s conditions (see the Introduction), this formula leads immediately to the fluctuation theorem for currents restated in terms of macroscopic forces (see page 124 in \( \Theta \)). In Section 6 we show that Fact \(3.3\) is a simple corollary of Fact \(3.1\). This was already pointed out in \( \Theta \), by different arguments.
3.2. **Fluctuation theorem for generalized currents associated to a basis of oriented cycles.** In this section, we extend the fluctuation theorem to currents referred to (what we call) a basis of oriented cycles in $G$. This answers a natural conceptual question. In addition, in applications, one can have identified a nice basis of oriented cycles and desire to work with it, without looking for a nice fundamental set of oriented cycles (see Section 4). First we fix some general concepts, applying some ideas of linear algebra to oriented cycles.

We say that the family of oriented cycles $C_1, \ldots, C_k$ in $G$ generates all the oriented cycles if for each oriented cycle $C$ there exist real numbers $a_1, \ldots, a_k$ satisfying $C = \sum_{i=1}^{k} a_i C_i$ (recall Definition 3.2). Such a generating set is called basis if it is minimal, in the sense that it does not contain a smaller generating subfamily. It is simple to check that minimality can be replaced by independence, i.e. there are not constants $a_1, \ldots, a_k$ (not all zero) such that $\sum_{i=1}^{k} a_i C_i = \emptyset$, where $\emptyset$ denotes the degenerate cycle with $S_\ell(\emptyset) = 0$ for each oriented edge $\ell$. In the last case, we also say that $C_1, \ldots, C_k$ are independent. Lemma 7.1 in the integrating Section 7 will report some very intuitive facts concerning bases, generating sets and independent sets. Here we recall that all bases have cardinality given by the chord number $s$, that any fundamental set of oriented cycles is a basis (the opposite implication is false, see Section 4) and that for each oriented cycle $C$ any fundamental set of oriented cycles is a basis (the opposite implication is false, see Section 7) and that for each oriented cycle $C$ the coefficients $a_1, \ldots, a_s$ in the decomposition

$$ C = \sum_{i=1}^{s} a_i C_i, \quad (3.10) $$

where $C_1, \ldots, C_s$ is a basis, are univocally determined. If the basis is not a fundamental set of oriented cycles the coefficients $a_1, \ldots, a_s$ do not have a simple geometric characterization as in (3.5). As showed in Section 7 if $C_1, \ldots, C_s$ is a basis and $C'_1, \ldots, C'_s$ is a fundamental set of oriented cycles with associated chords $\ell_1, \ldots, \ell_s$, then it holds

$$ (a_1, \ldots, a_s) = (S_{\ell_1}(C), \ldots, S_{\ell_s}(C)) B^{-1}, \quad B = (B_{ij})_{1 \leq i, j \leq s}, \quad B_{ij} = S_{\ell_j}(C_i). \quad (3.11) $$

Let us come back to our random walk on the graph $G$. We want to associate to each trajectory up to time $t$ an oriented cycle $C_t$. We do it as follows. Of the trajectory up to time $t$ we record the sequence of oriented bonds $(b_1, \ldots, b_n)$, $b_i \in E_o$, which the walker moves along, one after the other ($n$ is the number of jumps performed up to time $t$). We denote this path as reduced trajectory. Recall the definition of the function $N_\ell(t)$ given after (3.2). Note that $N_\ell(t)$ depends only on the reduced trajectory, since $N_\ell(t) = \sum_{i=1}^{n} \mathbb{1}(b_i = \ell) - \mathbb{1}(b_i = \ell)$. Given two different states $\sigma, \sigma'$ we fix a path $\gamma_{\sigma, \sigma'}$ in $G$ from $\sigma$ to $\sigma'$ specifying only the visited states and the edges along which the path evolves (there is no knowledge of jump times), i.e. $\gamma_{\sigma, \sigma'}$ is represented by a sequence of oriented bonds. We then introduce a random oriented cycle $C_t$ on $G$ as follows:

**Definition 3.4.** Fixed a family $\{\gamma_{\sigma, \sigma'}\}_{\sigma \neq \sigma'}$, let $(b_1, \ldots, b_n)$ be the reduced trajectory from $X_0$ to $X_t$. If $X_0 = X_t$ we define $C_t$ as the oriented cycle given by the
reduced trajectory itself, otherwise we define $C_t$ as the cycle $(b_1, \ldots, b_n, c_1, \ldots, c_r)$ where $\gamma_{X_0, X_t} = (c_1, \ldots, c_r)$.

We point out that

$$N_\ell(t) = S_\ell(C_t) + O(1) \quad \forall \ell \in E_0$$

(3.12)

where the errors $O(1)$ are uniformly bounded as $\ell$ varies in $E_0$ and $t$ varies in $[0, \infty)$.

From now on, we refer to a basis $C_1, \ldots, C_s$ and a family $\{\gamma_{\sigma, \sigma'}\}_{\sigma \neq \sigma'}$, fixed once and for all. Due to the above discussion, we know that the random numbers $a_1(t), \ldots, a_s(t)$ such that

$$C_t = \sum_{i=1}^s a_i(t)C_i,$$  

(3.13)

exist and are univocally determined. Note that these random numbers depend not only from the basis but also on the paths $\gamma_{\sigma, \sigma'}$. On the other hand, choosing other paths $\gamma_{\sigma, \sigma'}$ would change the random numbers $a_i(t)$ of quantities uniformly bounded as $t$ varies in $[0, \infty)$ (as a byproduct of (3.11) and (3.12)). We point out that, by (3.5) and (3.12), if our basis is a fundamental set of oriented cycles with associated chords $\ell_1, \ldots, \ell_s$, then it holds $a_i(t) = N_{\ell_i}(t) + O(1)$. In particular, a part an error of order $O(1)$, the number $a_i(t)$ is simply the flux along the chord $\ell_i$, which equals the time–integrated current along $\ell_i$. Due to this special case, we call $a_i(t)$ generalized time–integrated current.

We can finally state our fluctuation theorem:

**Theorem 3.5.** Fix a basis $C_1, \ldots, C_s$ and paths $\{\gamma_{\sigma, \sigma'}\}_{\sigma \neq \sigma'}$. Then, for any initial distribution $\nu$ and for any $\lambda_1, \ldots, \lambda_s \in \mathbb{R}$, the limit

$$Q_b(\lambda_1, \ldots, \lambda_s) := \lim_{t \to \infty} -\frac{1}{t} \ln \mathbb{E}_\nu \left[ e^{-\sum_{i=1}^s \lambda_i a_i(t)} \right]$$

exists, is finite and does not depend on $\nu$. Moreover, it holds

$$Q_b(\lambda_1, \ldots, \lambda_s) = Q_b(A(C_1) - \lambda_1, \ldots, A(C_s) - \lambda_s).$$

(3.15)

The index $b$ refers to the term “basis”. Due to the fact that $a_i(t) = N_{\ell_i}(t) + O(1)$ when the basis is a fundamental set of oriented cycles, the above result extends Fact 3.3. The proof of Theorem 3.5 is given in Section 7.1.

4. Applications to molecular motors moving along a polymer

In this section we consider a molecular motor [14] moving along a polymer (mathematically, a one dimensional periodic environment), under the effect of an external force $f$, using chemical energy to produce mechanical work. We write $\Delta \mu$ for the chemical potential difference associated to ATP hydrolysis. We denote by $x_t$ the position of the molecular motor along the filament and by $z_t$ the number of hydrolyzed ATPs minus the number of synthesized ATPs such that $z_0 = 0$. We want to apply Theorem 3.5 to prove in full generality the relation (1.2) described in the Introduction.
The above fluctuation relation [12] has been proved in [21] [22] for a special model with two chemical states. The method followed there relies on the manipulation of $2 \times 2$ matrices (since only two chemical states are considered there). On the other hand, keeping in mind the above observations concerning macroscopic forces and affinities, one would expect the above symmetry [12] to be universal. This is indeed what we prove below as confirmation of the large flexibility of the fluctuation theorem referred to oriented cycles. To deal with this problem in full generality one has to work with a very large graph.

First of all we need to fix a discrete kinetic model. The natural modeling of molecular motors is by continuous models called ratchet models [16] [28]. Methods to derive a discrete model from the continuous ratchet model have been developed in full generality (cf. [31] and reference therein), thus leading to the following class of kinetic models. The model is a continuous–time Markov chain with state space $\mathbb{Z} \times \Gamma$, $\Gamma$ being the finite set of the chemical states of the motor, with master equation

$$
\partial_t p_t(x, \sigma) = \omega^\sigma_{x-1, x} p_t(x-1, \sigma) + \omega^\sigma_{x+1, x} p_t(x+1, \sigma) - [\omega^\sigma_{x, x-1} + \omega^\sigma_{x, x+1}] p_t(x, \sigma)
$$

$$+ \sum_{\sigma' \neq \sigma} [\omega^\sigma_{\sigma' \sigma} p_t(x, \sigma') - \omega^\sigma_{\sigma' \sigma} p_t(x, \sigma)]. \quad (4.1)
$$

Above, $p_t(x, \sigma)$ denotes the probability of the motor to be at site $x \delta$ ($\delta$ being the length of spatial unity in the discretization) at time $t$ in chemical state $\sigma$. $\omega^\sigma_{x, x'}$ is the probability rate for a jump from the position $x \delta$ to $x' \delta$ (with $|x - x'| = 1$) if the chemical state is $\sigma$, and $\omega^\sigma_{\sigma' \sigma}$ is the probability rate for a chemical transition from $\sigma$ to $\sigma'$ if the mechanical coordinate is $x$. When considering motor proteins moving along polymeric filaments, the above rates are periodic function in $x$, with the same period.

In order to keep information about the ATP consumption, it is convenient to enrich the above discrete model, extending the state space and distinguishing between active and passive chemical transitions (i.e. related to hydrolysis/synthesis of ATP or to thermal noise) [27]. The new state of the system (motor plus environment) is now described by the triple $(x, \sigma, z) \in \mathbb{Z} \times \Gamma \times \mathbb{Z}$, where $z$ denotes the algebraic number of hydrolyzed ATP molecules (in the sense that $z$ increases of one unity for each ATP hydrolysis and decreases of one unity for each ATP synthesis). We write $\omega^{x, l}_{\sigma, \sigma'}$ for the probability rate of a chemical transition from $\sigma$ to $\sigma'$ at the mechanical state $x$ with the consumption of $l = -1, 0, 1$ ATP molecules. Hence, $\omega^{x, l}_{\sigma, \sigma'}$ is the probability rate for the jump $(x, \sigma, z) \rightarrow (x, \sigma', z + l)$. The other possible jumps are the mechanical ones $(x, \sigma, z) \rightarrow (x', \sigma, z)$, $|x - x'| = 1$, having probability rate $\omega^\sigma_{x, x'}$. The resulting master equation is the following:

$$
\partial_t p_t(x, \sigma, z) = \omega^\sigma_{x-1, x} p_t(x-1, \sigma, z) + \omega^\sigma_{x+1, x} p_t(x+1, \sigma, z) - [\omega^\sigma_{x, x-1} + \omega^\sigma_{x, x+1}] p_t(x, \sigma, z)
$$

$$+ \sum_{l=-1,0,1} \sum_{\sigma' \neq \sigma} [\omega^{x, l}_{\sigma' \sigma} p_t(x, \sigma', z + l) - \omega^{x, l}_{\sigma' \sigma} p_t(x, \sigma, z)]. \quad (4.2)
$$

In what follows, we suppose that all the rates are positive. In principle, this is not a restriction since positive but very small rates correspond to very unlikely transitions.
Recall that $f$ denotes the load force and $\Delta \mu$ the chemical potential difference associated to ATP hydrolysis. We write $V_\sigma$ for the potential energy of the molecular motor in the chemical state $\sigma$ due to the interaction with the polymer. Again, the functions $V_\sigma$, $\sigma \in \Gamma$, are periodic functions of the same period. The energy associated to the state $(x, \sigma, z)$ is given by

$$E(x, \sigma, z) = V_\sigma(x\delta) - fx\delta - z\Delta \mu + \text{const.}$$  \hspace{1cm} (4.3)

Then, the detailed balance condition reads

\[
\begin{align*}
\omega^\sigma_{x,x+1} / \omega^\sigma_{x+1,x} &= \exp \{-\beta[V_\sigma(x\delta + \delta) - V_\sigma(x\delta)] + \beta \delta f\}, \\
\omega^\sigma_{\sigma,\sigma'} / \omega^\sigma_{\sigma',\sigma} &= \exp \{-\beta[V_\sigma'(x\delta) - V_\sigma(x\delta)] + \beta \Delta \mu\}. \hspace{1cm} (4.4)
\end{align*}
\]

We can now formulate our result:

**Fact 4.1.** Recall that $x_t$, $z_t$ denote the position at time $t$ of the molecular motor and the total ATP consumption up to time $t$. Denote by $f \beta$ and $x_0$ the adimensional quantities $f \beta \times [1\text{m}]$ and $x_t/\text{[1m]}$ ($[1\text{m}]$ being the length unit). Then for any given initial configuration $(x_0, z_0 = 0, \sigma_0)$ and for any constants $\lambda, \gamma \in \mathbb{R}$ the following limit exists:

$$\vartheta(\lambda, \gamma) := \lim_{t \to \infty} -\frac{1}{t} \ln \mathbb{E}_{(x_0, z_0 = 0, \sigma_0)}[e^{-\lambda x_t - \gamma z_t}].$$  \hspace{1cm} (4.5)

Moreover, it holds

$$\vartheta(\lambda, \gamma) = \vartheta(f \beta - \lambda, \beta \Delta \mu - \gamma), \hspace{1cm} \lambda, \gamma \in \mathbb{R}. \hspace{1cm} (4.6)$$

We point out that the model presented in [18, 21, 22] is indeed a coarse-graining approximation of the model we have described above when considering two chemical states and suitable potentials.

### 4.1. Proof of Fact 4.1

In order to apply Theorem 3.5 we need to work with a finite state space. This is obtained by a suitable projection.

Recall that the filament is periodic. We define $N$ as the number of $\delta$–units contained in a spatial period. This implies in particular

\[
\begin{align*}
V_\sigma(x\delta) &= V_\sigma(x\delta + N\delta), \hspace{1cm} \omega^\sigma_{x,\sigma'} = \omega^\sigma_{x+N,\sigma'}, \\
\omega^\sigma_{x+1,x} &= \omega^\sigma_{x+N+1,x+N}, \hspace{1cm} \omega^\sigma_{x,x+1} = \omega^\sigma_{x+N,x+N+1}. \hspace{1cm} (4.7)
\end{align*}
\]

We write $\mathbb{Z}_N$ for the quotient space $\mathbb{Z}/N\mathbb{Z}$ given by integers modulo $N$. Of course, sums in $\mathbb{Z}_N$ are modulo $N$. Due to (4.7) both the potentials and the jump rates can be thought of with the spacial parameter $x$ varying in $\mathbb{Z}_N$.

We introduce a finite graph $\mathcal{G}$ with multiple edges and no loop, indicating the canonical orientation of edges. To this aim it is convenient to label the states in $\Gamma$ as $\sigma_1, \sigma_2, \ldots, \sigma_m$ ($m = |\Gamma|$). Then, the vertexes of $\mathcal{G}$ are given by the pairs $(x, \sigma_i)$, $x \in \mathbb{Z}_N$ and $1 \leq i \leq m$. We put an oriented edge $e^\sigma_{x,x+1}$ from state $(x, \sigma_i)$ to state $(x + 1, \sigma_i)$. Moreover, given $1 \leq i < j \leq m$, we put three oriented edges from state $(x, \sigma_i)$ to state $(x, \sigma_j)$ labeled by the index $l = -1, 0, 1$ and we call them $e^\sigma_{\sigma_i,\sigma_j}$. See figure [1]. Note that $\mathcal{G}$ has $Nm$ vertexes and $Nm + 3Nm(m - 1)/2$ edges. In particular, its chord number is

$$s = 3Nm(m - 1)/2 + 1.$$  \hspace{1cm} (4.8)
probability rate of the reversed jump is \( \omega_{x,x+1} \), while the probability rate for a jump along the edge \( e \) equals \( \omega_{e} \). Similarly, given \( 1 \leq i < j \leq m \) and \( l = -1, 0, 1 \), the probability rate for a jump along the edge \( e_{\sigma_i,\sigma_j} \) equals \( \omega_{e_{\sigma_i,\sigma_j}} \), while the probability rate of the reversed jump is \( \omega_{e_{\sigma_i,\sigma_j}} \). Recall that, given an oriented edge \( e \), we write \( N_e(t) \) for the number of times the random walk jumps along the edge \( e \) minus the number of times the random walk jumps along the reversed edge \( e \) up to time \( t \). Trivially, the above random walk \( X_t \) can be coupled with the Markov chain considered in the previous subsection getting the identities

\[
x_t/\delta = \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i \leq m} N_{e_{\sigma_i,x+1}}(t), \quad z_t = \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i \leq j \leq m} \left[ N_{e_{\sigma_i,\sigma_j}}(t) - N_{e_{\sigma_i,\sigma_j}^{-1}}(t) \right].
\]

This fact, together with (5.3), implies that the limit (4.5) exists and is finite, hence the function \( \vartheta(\lambda, \gamma) \) is well defined.

It remains to prove (4.6). To this aim recall how we have associated the cycle \( C_t \) to the trajectory of the random walk up to time \( t \) (see Definition 3.4). Trivially, a part an error of order one uniformly in \( t \in [0, \infty) \), the above identities can be rewritten as

\[
\begin{cases}
x_t/\delta = \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i \leq m} S_{e_{\sigma_i,x+1}}(C_t) + O(1), \\
z_t = \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i < j \leq m} \left[ S_{e_{\sigma_i,\sigma_j}}(C_t) - S_{e_{\sigma_i,\sigma_j}^{-1}}(C_t) \right] + O(1).
\end{cases}
\]

We give now two different applications of Theorem 3.5. In the first case we exhibit a nice basis which is not a fundamental set, in the second case we exhibit a spanning tree leading to a nice fundamental set.

4.1.1. A nice basis. We introduce a basis of oriented cycles on \( G \). We call \( C_0 \) the cycle described by the ordered family of oriented edges

\[
C_0 = (e_{\sigma_1,\sigma_2}, e_{\sigma_2,\sigma_3}, \ldots, e_{\sigma_{m-1},\sigma_m}, e_{\sigma_m,\sigma_1}).
\]

Given \( x \in \mathbb{Z}_N \) and \( 1 \leq i < j \leq m \), we introduce the three oriented cycles (see figure 2)

\[
\begin{align*}
C_{\sigma_i,\sigma_j}^{x,-1} &= (e_{\sigma_i,\sigma_j}^{x,0}, e_{\sigma_i,\sigma_j}^{x,-1}), \\
C_{\sigma_i,\sigma_j}^{x,1} &= (e_{\sigma_i,\sigma_j}^{x,1}, e_{\sigma_i,\sigma_j}^{x,0}).
\end{align*}
\]
\[ C_{x,x+1}^{x,x+1} = (e_{x,x+1}^{x,x+1}, e_{x,x+1}^{x,x+1}, e_{x,x+1}^{x,x+1}). \]

\[ C_{x,x-1}^{x,x-1} = C_{x,x}^{x,x} = C_{x,x+1}^{x,x+1}. \]

**Figure 2.** The cycles \( C_{x,x-1}^{-1}, C_{x,x}^{1}, C_{x,x+1}^{x,x+1} \).

Consider now, for each \( x \), the complete graph on the set \( \{(x, \sigma_i) : 1 \leq i \leq m \} \) with canonically oriented edges \( e_{x,0}^{x,0} \), \( 1 \leq i < j \leq m \) (see figure 3). Trivially, the edges \( e_{x,0}^{x,0}, e_{x,0}^{x,0}, \ldots, e_{x,0}^{x,0} \) form a spanning tree. We call \( C_{x,x}^{x,x} \) the oriented cycle associated to the chord \( e_{x,0}^{x,0} \), with \( (i, j) \notin \{(1, 2), (2, 3), \ldots, (m-1, m)\} \). The orientation of \( C_{x,x}^{x,x} \) agrees with the one of the chord \( e_{x,0}^{x,0} \).

**Figure 3.** The complete graph with edges \( e_{x,0}^{x,0}, 1 \leq i < j \leq m := 4 \).

**Lemma 4.2.** Consider the family of oriented cycles

(i) \( C_0 \),
(ii) \( C_{x,x}^{-1} \) with \( x \in \mathbb{Z}_N \) and \( 1 \leq i < j \leq m \),
(iii) \( C_{x,x}^{1} \) with \( x \in \mathbb{Z}_N \) and \( 1 \leq i < j \leq m \),
(iv) \( C_{x,x}^{x,x} \) with \( x \in \mathbb{Z}_N \), \( 1 \leq i < j \leq m \) and \( (i,j) \notin \{(1,2), (2,3), \ldots, (m-1,m)\} \),
(v) \( C_{x,x}^{x,x+1} \) with \( x \in \mathbb{Z}_N \) and \( 1 \leq i \leq m-1 \).

Then the above family of oriented cycles is a basis.

**Proof.** The oriented cycles of type (i),(ii),...,(v) are respectively 1, \( Nm(m-1)/2 \), \( Nm(m-1)/2 \), \( Nm(m-1)/2 - N(m-1) \), \( N(m-1) \). It follows then that the above
family of oriented cycles has cardinality $3Nm(m - 1)/2 + 1$, which is the chord number $s$ given in (4.8).

By point (v) in Lemma 7.1 in order to show that it is a basis it is enough to prove independence. Suppose to have a linear combination of the above oriented cycles which equals the degenerate cycle $0$. First we observe that the edge $e_{x_i, x_j}^{-1}$ belongs only to $C_{x_i, x_j}^{-1}$, the reversed edge does not belong to any oriented cycle in the family. By applying the operator $S_\ell$ with $\ell = e_{x_i, x_j}^{-1}$, and then varying $x, i, j$, we get that the cycles of type (ii) do not appear in the linear combination. The same holds for cycles of type (iii) (think to the edges $e_{x_i, x_j}^{x_i, x_j}$). Keeping in mind this consideration, the edge $e_{x_i, x_j}^{x_i, x_j}$ with $x \in \mathbb{Z}_N$, $1 \leq i < j \leq m$ and $(i, j) \notin \{(1, 2), (2, 3), \ldots, (m - 1, m)\}$, appears only in the oriented cycle $C_{x_i, x_j}^{x_i, x_j}$ of type (iv) while its reversed edge does not appear in any cycle of the family (recall the properties of a fundamental set of oriented cycles). Note that edges of the forms $e_{x_i, x_j}^{x_i, x_j}$ or $e_{x_i, x_j}^{x_i, x_j}$ appear in the oriented cycles of type (v) but it must be $j = i + 1$.

At this point, we know that the linear combination involves only $C_0$ and the oriented cycles of type (v), i.e. we have

$$\alpha_0 C_0 + \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i < m} \alpha_{\sigma_i, \sigma_{i+1}} x_{\sigma_i, \sigma_{i+1}}^x = 0. \tag{4.10}$$

Applying to both members the operator $S_\ell$ with $\ell = e_{x_i, x_j}^{x_i, x_j}$ ($x \in \mathbb{Z}_N$ and $1 \leq i \leq m$), we get for any $x \in \mathbb{Z}_N$

$$\begin{cases} 
\alpha_0 + \alpha_{\sigma_i, \sigma_1} x_{\sigma_i, \sigma_2}^x = 0 \\
\alpha_{\sigma_i, \sigma_{i+1}} x_{\sigma_{i+1}, \sigma_2}^x = \alpha_{\sigma_{i+1}, \sigma_{i+2}} x_{\sigma_{i+1}, \sigma_2}^x \\
\alpha_{\sigma_{m-1}, \sigma_m} = 0.
\end{cases} \tag{4.11}$$

The above system trivially implies that all coefficients in (4.10) are zero. Hence, the oriented cycles in the above family are independent. \hfill \square

We point out that the above basis is not a fundamental set of oriented cycles. Indeed, each edge of $C_0$ belongs also to some oriented cycle of type (v), hence $C_0$ can not contain any chord.

Let us now compute the affinities associated to the oriented cycles in our basis. Due to the detailed balance relations (4.14), we have the following weights:

$$\begin{align*}
\left\{ \begin{array}{l}
w(x_{\sigma_i, \sigma_{i+1}}^x) = -\beta \left[ V_{\sigma_i}(x\delta + \delta) - V_{\sigma_i}(x\delta) \right] + \beta \delta f, \\
w(e_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = -\beta \left[ V_{\sigma_i}(x\delta) - V_{\sigma_i}(x\delta) \right] + \beta \Delta \mu.
\end{array} \right. \tag{4.12}
\end{align*}$$

Hence,

$$A(C_0) = \beta N f \delta, \quad A(C_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = \beta \Delta \mu, \quad A(C_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = \beta \Delta \mu, \quad A(C_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = \beta \Delta \mu, \quad A(C_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = \beta \Delta \mu, \quad A(C_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = \beta \Delta \mu, \quad A(C_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = \beta \Delta \mu, \quad A(C_{\sigma_i, \sigma_{i+1}}^{x_i, x_i}) = \beta \Delta \mu.$$

(4.13)
(note that conservative force fields never appear in the cycle affinities). We write

$$C_t = a_0(t)C_0 + \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i < j \leq m} \left( a^{x,-1}_{\sigma_i,\sigma_j}(t)C^{x,-1}_{\sigma_i,\sigma_j} + a^{x,1}_{\sigma_i,\sigma_j}(t)C^{x,1}_{\sigma_i,\sigma_j} \right) + \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i < j \leq m} a^{x,0}_{\sigma_i,\sigma_j}(t)C^{x,0}_{\sigma_i,\sigma_j} + \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i < m} a^{x,x+1}_{\sigma_i,\sigma_{i+1}}(t)C^{x,x+1}_{\sigma_i,\sigma_{i+1}}.$$  \hspace{1cm} (4.14)

By applying (4.9) to the above decomposition and setting $\delta = \delta/\lfloor 1m \rfloor$, we get that

$$\lambda \bar{x}_t + \gamma z_t = \lambda N \tilde{\delta} a_0(t) + \gamma \sum_{x \in \mathbb{Z}_N} \sum_{1 \leq i < j \leq m} \left[ a^{x,-1}_{\sigma_i,\sigma_j}(t) + a^{x,1}_{\sigma_i,\sigma_j}(t) \right] + O(1). \hspace{1cm} (4.15)$$

The above identity together with Theorem 3.5 implies that

$$\vartheta(\lambda, \gamma) = Q_b(C_0 \to \lambda N \tilde{\delta}, C^{x,-1}_{\sigma_i,\sigma_j} \to \gamma, C^{x,1}_{\sigma_i,\sigma_j} \to \gamma, C^{x,0}_{\sigma_i,\sigma_j} \to 0, C^{x,x+1}_{\sigma_i,\sigma_{i+1}} \to 0) = Q_b(C_0 \to \beta N f \delta - \lambda N \tilde{\delta}, C^{x,-1}_{\sigma_i,\sigma_j} \to \beta \Delta \mu - \gamma, C^{x,1}_{\sigma_i,\sigma_j} \to \beta \Delta \mu - \gamma, C^{x,0}_{\sigma_i,\sigma_j} \to 0, C^{x,x+1}_{\sigma_i,\sigma_{i+1}} \to 0) = \vartheta(\beta f - \gamma, \beta \Delta \mu - \gamma). \hspace{1cm} (4.16)$$

This concludes the proof of Fact 4.6.

4.1.2. A nice fundamental set. The above arguments can be applied also to fundamental sets of oriented cycles. As example of spanning tree, one can take the tree given by the edges $e^{x,0}_{\sigma_i,\sigma_j}$ with $2 \leq i \leq m$ and $x \in \mathbb{Z}_N$, and $e^{x,1}_{x,x+1}$ with $1 \leq x \leq N - 1$ (see figure 4). Alternatively, one can take as spanning tree the one given by the edges $e^{1,0}_{\sigma_i,\sigma_j}$ with $(i, j) \in \{(1, 2), (2, 3), \ldots, (m-1, m)\}$, and $e^{x,1}_{x,x+1}$ with $1 \leq i \leq m$ and $1 \leq x \leq N - 1$. In both cases, the associated fundamental set is tractable. The advantage here is that one does not have to check that the associated fundamental set is a basis, since this is automatically. We leave the details to the interested reader.

![Figure 4](image-url)

**Figure 4.** Example of spanning tree where $N = 3$, $m = 4$. The spanning tree is in boldface, edges $e^{x,1}_{\sigma_i,\sigma_j}$ have been omitted.
5. Mathematical Integration to Section 2

The decomposition of the generator \( L \) in terms of the rates \( k^{(i)}(\sigma, \sigma') \) described in Section 2 is naturally associated to the following construction of the Markov chain \( X_t \). First we observe that the evolution of the Markov chain is univocally determined by the sequence \( \sigma_0, \sigma_1, \sigma_2, \ldots \) of the visited states (listed in chronological order) and by the times \( T_n, n \in \mathbb{N} \), of the \( n \)-th jump (with the convention \( T_0 = 0 \)). In order to specify these last quantities, we consider a family of independent exponential random variables \( T^{(i,n)}_{\sigma,\sigma'} \), parameterized by the integers \( n \in \mathbb{N} \) and \( i : 1 \leq i \leq m \) and by the ordered pairs \((\sigma, \sigma')\) of distinct elements in \( S \). The random variables \( T^{(i,n)}_{\sigma,\sigma'} \) are all defined on a same probability space \((\Omega, \mathcal{F}, \mathbb{P})\), \( T^{(i,n)}_{\sigma,\sigma'} \) is an exponential random variable with parameter (i.e. 1/mean) \( k^{(i)}(\sigma, \sigma') \). Note that \( T^{(i,n)}_{\sigma,\sigma'} = \infty \) if \( k^{(i)}_{\sigma,\sigma'} = 0 \).

The Markov chain \( X_t \) starting in \( \sigma_0 \) can be inductively constructed as follows as function on the space \( \Omega \): known the \( n \)-th jump time \( T_n \) and the \( n \)-th visited state \( \sigma_n \), we set \( T^{(n)} = \min_{i, \sigma'} T^{(i,n)}_{\sigma_n, \sigma'} \). Then \( T_{n+1} := T_n + T^{(n)} \), i.e. after the \( n \)-th jump the Markov chain remains at \( \sigma_n \) for a time \( T^{(n)} \), after that it jumps to the state \( \sigma' \) such that for some \( i \) it holds \( T^{(n)} = T^{(i,n)}_{\sigma_n, \sigma'} \). As well known (cf. [24][Theorem 2.3.3]), the index \( i \) and the state \( \sigma' \) such that \( T^{(n)} = T^{(i,n)}_{\sigma_n, \sigma'} \) are univocally determined a.s.

Recall the interpretation of the Markov chain as random walk on the graph \( \mathcal{G} \), given in Section 2. Known \( \sigma_n \) and \( T_n \), we can think that the walker moves at time \( T_{n+1} = T_n + T^{(n)} \) to the state \( \sigma' \) along the \( i \)-edge if \( T^{(n)} = T^{(i,n)}_{\sigma_n, \sigma'} \). In addition, recall that in Section 2 given the initial distribution \( \nu \) on \( S \), we have defined \( \mathbb{P}_\nu \) as the probability measure describing the evolution of the Markov chain keeping knowledge of the crossed edges. We point out that \( \mathbb{P}_\nu \) is a probability measure on the space \( \Omega \), where all the exponential variables \( T^{(i,n)}_{\sigma,\sigma'} \) are defined.

5.1. Proof of Theorem 2.1. The proof follows the strategy stated in [24][Section 2.3], i.e. one has simply to extend the proof given in [24][Section 2.1] for \( m = 1 \). The only difference is that one has to keep in mind the special construction of the Markov chain \( X_t \) given above. We give the proof for completeness and also to show that the assumptions required in [24][Section 2.3] are redundant.

We fix \( \lambda_1, \ldots, \lambda_m \) and set \( g(t) = \mathbb{E}_\sigma \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(t)} \right] \). It is well known that the function \( \mathbb{R} \ni t \to g(t) \in (0, \infty) \) is differentiable. We think of \( X_t \) as a random walk on the graph \( \mathcal{G} \) with multiple edges and no loop as explained in Section 2.

Fixed \( \varepsilon > 0 \) we introduce the following events: \( A \) is the event that in the time interval \( [0, \varepsilon] \) the walker does not jump, \( B^{(i)}_{\sigma,\sigma'} \) is the event that in the time interval \( [0, \varepsilon] \) the walker makes a unique jump and this jump takes place along the \( i \)-labelled edge from \( \sigma \) to \( \sigma' \), while \( C \) denotes the event that neither \( A \) nor any event \( B^{(i)}_{\sigma,\sigma'} \).
takes place. By the Markov property we can write
\[ g_{t+\varepsilon}(\sigma) = \mathbb{E}_\sigma \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(\varepsilon)} g_t(\sigma_\varepsilon) \right] = \mathbb{E}_\sigma \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(\varepsilon)} g_t(\sigma_\varepsilon); A \right] + \sum_{\sigma' : \sigma' \neq \sigma} \mathbb{E}_\sigma \left[ e^{-\sum_{j=1}^m \lambda_j W^{(j)}(\varepsilon)} g_{t}(\sigma_\varepsilon); B^{(i)}_{\sigma, \sigma'} \right] + \mathbb{E}_\sigma \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(\varepsilon)} g_t(\sigma_\varepsilon); C \right]. \]

Using that \( P_\sigma(A) = 1 - r(\sigma)\varepsilon + o(\varepsilon), P_\sigma(B^{(i)}_{\sigma, \sigma'}) = k^{(i)}(\sigma, \sigma')\varepsilon + o(\varepsilon) \) and \( P_\sigma(C) = o(\varepsilon) \), the above expansion (5.1) implies that
\[ \frac{dg_t}{dt}(\sigma) = \sum_{\sigma' : \sigma' \neq \sigma} \left[ \sum_{i:1 \leq i \leq m} \frac{k^{(i)}(\sigma, \sigma') - \lambda_i k^{(i)}(\sigma', \sigma)}{k^{(i)}(\sigma, \sigma') > 0} \lambda_i \right] g_t(\sigma') - r(\sigma) g_t(\sigma) =: (L_\lambda g_t)(\sigma). \]

The above differential equation and the fact that \( g_0(\sigma) = 1 \) for any \( \sigma \) imply that \( g_t(\sigma) = (e^{t L_\lambda} g_0)(\sigma) = \sum_{\sigma' \in S} [e^{t L_\lambda}]_{\sigma, \sigma'}^0. \) In particular, we can write
\[ \mathbb{E}_\nu \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(t)} \right] = (\nu, e^{t L_\lambda} 1), \]

where \((\cdot, \cdot)\) denotes the Euclidean scalar product in \( \mathbb{R}^S \) and 1 denotes the vector with all entries equal to 1.

We point out that the \( L_\lambda \) has off-diagonal nonnegative entries. In particular, for \( a \) large enough, \( M := L_\lambda + aI \) has nonnegative entries and one can apply to it the Perron–Frobenius theorem (cf. [15] Theorem 1.5.4]. From the fact that \( X_t \) is an irreducible Markov chain, we derive that \( L_\lambda \) is irreducible (i.e. given \( \sigma \neq \sigma' \) there exists a path \( \sigma = \sigma_0, \sigma_1, \ldots, \sigma_n = \sigma' \) such that \( [L_\lambda]_{\sigma_j, \sigma_{j+1}} > 0 \) for all \( j : 0 \leq j < n \) and as a consequence the same conclusion holds for \( M \). Applying now the Perron–Frobenius theorem we conclude that \( M \) has a maximal eigenvalue which is simple and is associated to an eigenvector \( v \) having all positive entries. Hence, the same conclusion holds for \( L_\lambda \). We call \(-e(\Delta)\) the maximal eigenvalue of \( L_\lambda \) associated to \( v \). We write \( v_j \) for the \( j \)-th entry of \( v \) and set \( v_{\max} = \max_j v_j, v_{\min} = \min_j v_j \). Since both the vectors \( v, \nu \) and the matrix \( e^{t L_\lambda} = e^{-t a} e^{t M} \) has only nonnegative entries, we conclude that
\[ v_{\min}^{-1} e^{-te(\Delta)}(\nu, v) = v_{\max}^{-1} (\nu, e^{t L_\lambda} v) \leq (\nu, e^{t L_\lambda} 1) = \mathbb{E}_\nu \left[ e^{-\sum_{i=1}^m \lambda_i W^{(i)}(t)} \right] \leq v_{\min}^{-1} (\nu, e^{t L_\lambda} v) = v_{\min}^{-1} e^{-te(\Delta)}(\nu, v). \] Since \((\nu, v) > 0\) the above estimate trivially implies (5.3).
Since $L^\ast_{(1-\lambda_1,\ldots,1-\lambda_m)} = L_{(\lambda_1,\ldots,\lambda_m)}$ (the l.h.s. denotes the transposed matrix, recall the definition of $L^\ast$) and since $L^\ast_{(1-\lambda_1,\ldots,1-\lambda_m)}$ and $L_{(1-\lambda_1,\ldots,1-\lambda_m)}$ have the same eigenvalues, we immediately get (2.6).

□

6. Derivation of Fact 3.3 from Theorem 2.1

Recall that we have labeled the canonical oriented edges in $E_c$ as $\ell_1, \ell_2, \ldots, \ell_s, \ell_{s+1}, \ldots, \ell_n$, where $\ell_1, \ldots, \ell_s$ are the chords. Due to Definition 3.1 we list some simple properties concerning linear combinations of oriented cycles:

We list some simple properties concerning linear combinations of oriented cycles:

\begin{equation}
q\{\lambda_{\ell} : \ell \in E_c\} := \lim_{t \to \infty} \frac{1}{t} \ln E_{\nu} \left[ e^{-\sum_{\ell \in E_c} \lambda_{\ell} N_\ell(t)} \right] = \lim_{t \to \infty} \frac{1}{t} \ln E_{\nu} \left[ e^{-\sum_{\ell \in E_c} \lambda_{\ell} S_{\ell}(G_\ell)} \right].
\end{equation}

Due to (3.5) (recall the definition (3.2) of the weight $w(\ell)$) we can write

\begin{align*}
\sum_{i=1}^s \lambda_i S_{\ell_i}(G_\ell) &= \sum_{i=1}^s \lambda_i S_{\ell_i}(G_\ell) + \sum_{i=s+1}^n w(\ell_i) S_{\ell_i}(G_\ell) - \sum_{i=s+1}^n w(\ell_i) S_{\ell_i}(G_\ell) \\
&= \sum_{i=1}^s \lambda_i S_{\ell_i}(G_\ell) + \sum_{i=s+1}^n w(\ell_i) S_{\ell_i}(G_\ell) - \sum_{i=s+1}^n \sum_{j=1}^n w(\ell_i) S_{\ell_j}(G_\ell) S_{\ell_i}(G_\ell)
\end{align*}

\begin{align*}
&= \sum_{i=1}^s \left[ \lambda_i - \sum_{a=s+1}^n w(\ell_a) S_{\ell_a}(G_\ell) \right] S_{\ell_i}(G_\ell) + \sum_{i=s+1}^n w(\ell_i) S_{\ell_i}(G_\ell).
\end{align*}

The above identity and (6.1) imply that the limit (3.8) exists, is finite and equals

\begin{equation}
Q(\lambda_1, \ldots, \lambda_s) = q\{\lambda_i - \sum_{a=s+1}^n w(\ell_a) S_{\ell_a}(G_\ell)\}_{1 \leq i \leq s, \{w(\ell_i)\}_{s+1 \leq i \leq n}}.
\end{equation}

Due to the fluctuation relation (3.4), the expression in the r.h.s. equals

\begin{equation}
q\{-\lambda_i + w(\ell_i) + \sum_{a=s+1}^n w(\ell_a) S_{\ell_a}(G_\ell)\}_{1 \leq i \leq s, \{0\}_{s+1 \leq i \leq n}}.
\end{equation}

As already observed, given $i : 1 \leq i \leq s$, $S_{\ell_j}(G_\ell) = \delta_{i,j}$ for $1 \leq i, j \leq s$. In particular, $w(\ell_i) + \sum_{a=s+1}^n w(\ell_a) S_{\ell_a}(G_\ell)$ simply equals the affinity $A(G_\ell)$. Combining this observation with the above identities, we get that

\begin{equation}
(6.2) = q\{A(G_\ell) - \lambda_1\}_{1 \leq i \leq s, \{0\}_{s+1 \leq i \leq n}} = Q(\{A(G_\ell) - \lambda_1\}_{1 \leq i \leq s}).
\end{equation}

This completes the proof of Fact 3.3. □

7. Mathematical integration to Subsection 3.2

We list some simple properties concerning linear combinations of oriented cycles:

Lemma 7.1. The following holds:

(i) any generating set of oriented cycles has cardinality at least the chord number $s$,

(ii) any independent set of oriented cycles has cardinality at most $s$. 
(iii) any basis has cardinality \( s \),
(iv) any generating set of oriented cycles of cardinality \( s \) is a basis,
(v) given a basis \( C_1, \ldots, C_s \) and given an oriented cycle \( C \), the coefficients \( a_1, \ldots, a_s \) such that \( C = \sum_{i=1}^{s} a_i C_i \) are univocally determined,
(vi) any fundamental set of oriented cycles is a basis.

Proof. We first prove (i), taking a generating set of oriented cycles \( C_1, \ldots, C_k \). Then we fix a fundamental set of oriented cycles \( C'_1, \ldots, C'_s \) and call \( \ell_1, \ldots, \ell_s \) the associated chords. We introduce the \( k \times s \) matrix \( B \) with \( B_{ij} = S_{\ell_j}(C_i) \). Due to (3.5) it holds \( C_i = \sum_{j=1}^{s} B_{ij} C'_j \) for all \( i : 1 \leq i \leq k \). On the other hand, by definition of generating set, there exists a \( s \times k \) matrix \( A \) such that \( C'_j = \sum_{i=1}^{k} A_{ji} C_i \) for all \( j : 1 \leq j \leq s \). Then, for all \( r : 1 \leq r \leq s \), it holds

\[
\delta_{jr} = S_{\ell_r}(C'_j) = \sum_{i=1}^{k} A_{ji} S_{\ell_r}(C_i) = \sum_{i=1}^{k} A_{ji} B_{ir}.
\]

The above relations can be rewritten as \( I = AB \), where \( I \) denotes the \( s \times s \) identity matrix. This trivially implies that \( B \) must have rank at least \( k \), hence \( k \geq s \).

In order to prove (ii) suppose that \( C_1, \ldots, C_k \) is an independent set of oriented cycles. Taking a fundamental set \( C'_1, \ldots, C'_s \) as above, for a suitable \( k \times s \) matrix we can write \( C_i = \sum_{j=1}^{s} B_{ij} C'_j \) for all \( i : 1 \leq i \leq k \). If \( k > s \), then we could find a non trivial zero linear combination of the rows of \( B \), i.e. not all zero coefficients \( a_1, \ldots, a_k \) such that \( \sum_{i=1}^{k} a_i B_{ij} = 0 \) for all \( j : 1 \leq j \leq s \). Since \( \sum_{i=1}^{k} a_i S_{\ell_i}(C_i) = \sum_{i=1}^{k} \sum_{j=1}^{s} a_i B_{ij} S_{\ell_i}(C'_j) \), this fact trivially implies that \( \sum_{i=1}^{k} a_i C_i = 0 \), in contradiction with the hypothesis of independence. This completes the proof of point (ii).

We can directly prove point (v). To this aim suppose that \( k = s \). Then, as argued above, independence implies that the above matrix \( B \) has rank \( s \), hence it is invertible. Calling \( A := B^{-1} \), since \( C_i = \sum_{j=1}^{s} B_{ij} C'_j \), this trivially implies that \( \sum_{j=1}^{s} A_{ji} C_i = C'_k \), for all \( k : 1 \leq k \leq s \). In particular, the family \( C_1, \ldots, C_k \) generates a fundamental set of oriented cycles which generates all oriented cycles by (3.5).

Point (iii) is an immediate consequence of (i) and (ii). To prove point (iv), let \( C_1, \ldots, C_s \) be a generating set of cardinality \( s \). If these cycles were dependent, then we could find a generating subset of oriented cycles, in contradiction with point (i). Property (vi) follows from the definition of basis, while property (vii) follows from (iv) and (3.5).

We point out that not any basis is a fundamental set of oriented cycles. Consider figure 5. Vertexes are numbered from 1 to 6. Consider the oriented cycles \( C_1 = 1 \rightarrow 2 \rightarrow 5 \rightarrow 6 \rightarrow 1 \), \( C_2 = 2 \rightarrow 3 \rightarrow 4 \rightarrow 5 \rightarrow 2 \), \( C_3 = 3 \rightarrow 4 \rightarrow 6 \rightarrow 1 \rightarrow 3 \) and \( C_4 = 4 \rightarrow 5 \rightarrow 6 \rightarrow 4 \) (above we have indicated the visited vertexes, in order of visit). This family is a basis. Indeed, it has cardinality given by the chord number and moreover it trivially generates the fundamental set of oriented cycles associated to the maximal tree given by the edges \( \{1, 2\}, \{1, 3\}, \{1, 6\}, \{4, 6\}, \{5, 6\} \) depicted in the figure by boldface (with exception of the edge \( \{1, 3\} \)). On the other hand
$C_1, \ldots, C_4$ do not form a fundamental set of oriented cycles since each edge of $C_4$ belongs (with the same or with opposite orientation) to some other oriented cycle $C_i, i \neq 4$. Hence, no edge of $C_4$ could be the chord associated to a hypothetical maximal tree.

Figure 5. Graph for an example of basis which is not a fundamental set.

We conclude this section with the proof of Theorem 3.5:

7.1. Proof of Theorem 3.5. We fix a fundamental set of oriented cycles $C'_1, \ldots, C'_s$ and call $\ell_1, \ldots, \ell_s$ the associated chords. Recall that the orientations of $C'_i$ and $\ell_i$ agree. We introduce the $s \times s$ matrix $B$ defined as $B_{ij} = S_{\ell_j}(C_i)$. Then by (3.5) it holds $C_j = \sum_{i=1}^s B_{ij} C'_i$. We point out that the matrix $B$ is invertible (see the arguments used in the proof of Lemma 7.1).

Given an oriented cycle $C$ we can express the coefficients $a_i$ in the representation $C = \sum_{i=1}^s a_i C_i$ by means of the fundamental set of oriented cycles and associated chords as follows. Applying the operator $S_{\ell_j}$ to the identity $C = \sum_{i=1}^s a_i C_i$, we get

$$S_{\ell_j}(C) = \sum_{i=1}^s a_i S_{\ell_j}(C_i) = \sum_{i=1}^s a_i B_{ij}, \quad j = 1, \ldots, s.$$  \hfill (7.1)

This implies that

$$(a_1, \ldots, a_s) = (S_{\ell_1}(C), \ldots, S_{\ell_s}(C)) B^{-1}. \hfill (7.2)$$

Writing $< \cdot, \cdot >$ for the scalar product in $\mathbb{R}^s$ and denoting by $S(t)$ the column vector with entries $S_{\ell_1}(C_t), \ldots, S_{\ell_s}(C_t)$, the above equation (7.2) applied to the oriented cycle $C_t$ gives $\sum_{i=1}^s a_i(t) \lambda_i = < S(t), B^{-1} \lambda >$. In particular, the expectation in (3.14) can be written as

$$\mathbb{E}_\nu \left[ e^{-\sum_{i=1}^s \lambda_i a_i(s)} \right] = \mathbb{E}_\nu \left[ e^{-< S(t), B^{-1} \lambda >} \right].$$

By the above identity, the representation (3.12) and Fact 3.3 we get that the limit in (3.14) exists and it holds $Q_b(\lambda) = Q(B^{-1} \lambda)$. Applying the fluctuation relation (3.9) and afterwards again the identity $Q_b(\cdot) = Q(B^{-1} \cdot)$, we get

$$Q_b(\lambda) = Q(B^{-1} \lambda) = Q(A - B^{-1} \lambda) = Q_b(B(A - B^{-1} \lambda)) = Q_b(B A - \lambda),$$
where $\mathcal{A}$ denotes the column vector with entries the affinities $\mathcal{A}(C'_1), \ldots, \mathcal{A}(C'_s)$. To conclude, it is enough to note that

$$(BA)_i = \sum_{j=1}^{s} B_{ij} \mathcal{A}(C'_j) = \sum_{j=1}^{s} S_{\ell_j}(C_i) \mathcal{A}(C'_j) = \sum_{j=1}^{s} S_{\ell_j}(C'_j) \left[ \sum_{\ell \in E_c} S_{\ell}(C'_j) w(\ell) \right] = \sum_{\ell \in E_c} w(\ell) \left[ \sum_{j=1}^{s} S_{\ell_j}(C_i) S_{\ell}(C'_j) \right] = \sum_{\ell \in E_c} w(\ell) S_{\ell}(C_i) = \mathcal{A}(C_i).$$

**Acknowledgements:** The authors thank L. Bertini and D. Gabrielli for useful discussions. A.F. acknowledges the financial support of the European Research Council through the “Advanced Grant” PTRELSS 228032.

**References**

[1] D. Andrieux, P. Gaspard, *Fluctuation theorems and the nonequilibrium thermodynamics of molecular motors*. Phys. Rev. E **74**, 011906 (2006).
[2] D. Andrieux, P. Gaspard, *Fluctuation theorem for transport in mesoscopic systems*. J. Stat. Mech.: Theory and Experiment, P01011 (2006).
[3] D. Andrieux, P. Gaspard, *Fluctuation theorem for currents and Schnakenberg network theory*. J. Stat. Phys. **127**, 107–131 (2007).
[4] D. Andrieux, P. Gaspard, *A fluctuation theorem for currents and non–linear response coefficients*. J. Stat. Mech.: Theory and Experiment, P02006 (2007).
[5] D. Andrieux, P. Gaspard, *Network and thermodynamic conditions for a single macroscopic current fluctuation theorem*. Comptes Rendus Physique **8**, 579–590 (2007).
[6] L. Bertini, G. Di Gesù, *Small noise asymptotic of the Gallavotti–Cohen functional for diffusion processes*. Preprint (2010).
[7] N. Biggs, *Algebraic graph theory*. Cambridge, Cambridge University Press, 1974.
[8] C. Bustamante, J. Liphardt, F. Ritort, *The nonequilibrium thermodynamics of small systems*. Physics Today **58**, 43–48 (2005).
[9] T. De Donder, P. Van Rysselberghe, *Affinity*. Stanford University Press, Menlo Park CA (1936).
[10] G. Gallavotti, E.G.D. Cohen, *Dynamical ensembles in stationary states*. J. Stat. Phys. **80**, 931–970 (1995).
[11] G. Gallavotti, *Extension of Onsager’s reciprocity to large fields and the chaotic hypothesis*. Phys. Rev. Lett. **77**, 4334–4337 (1996).
[12] P. Gaspard, *Fluctuation theorems for nonequilibrium reactions*. Journal of Chemical Physics **120**, 8898–8905 (2004).
[13] T.L. Hill, *Free Energy Transduction and Biochemical Cycle Kinetics*. Dover Publications Inc., New York, 2004.
[14] J. Howard, *Mechanics of motor proteins and the cytoskeleton*. Sunderland, Sinauer Associates Inc., 2001.
[15] D.-J. Jiang, M. Qian, M.-P. Qian, *Mathematical theory of nonequilibrium steady states*. Lecture Notes in Mathematics **1833**. Berlin, Springer Verlag, 2004.
[16] F. Jülicher, A. Ajdari, J. Prost, *Modeling molecular motors*. Rev. Mod. Phys. **69**, 1269–1281 (1997).
[17] A.B. Kolomeisky, M.E. Fisher, *Molecular motors: a theorist’s perspective*. Annu. Rev. Phys. Chem. **58**, 675–695 (2007).
[18] A.B. Kolomeisky, B. Widom, *A simplified ”ratchet” model of molecular motors*. J. Stat. Phys. **93**, 633–645 (1998).
[19] J. Kurchan, Fluctuation theorem for stochastic dynamics. J. Phys. A.: Math. Gen. 31 3719–3729 (1998).
[20] D. Lacoste, K. Mallick, Fluctuation relations for molecular motors. B. Duplantier and V. Rivasseau (eds), “Biological Physics. Poincaré Seminar 2009”, Progress in Mathematical Physics Vol. 60, Birkhäuser Verlag, Basel, 2011.
[21] D. Lacoste, A.W.C. Lau, K. Mallick, Non-equilibrium fluctuations and mechanochemical couplings of a molecular motor. Phys. Rev. Lett. 99, 158102 (2007).
[22] D. Lacoste, A.W.C. Lau, K. Mallick, Fluctuation theorem and large deviation function for a solvable model of a molecular motor. Phys. Rev. E 78, 011915 (2008).
[23] D. Lacoste, K. Mallick, Fluctuation Theorem for the flashing ratchet model of molecular motors. Phys. Rev. E 80, 021923 (2009).
[24] J.L. Lebowitz, H. Spohn, A Gallavotti–Cohen-type symmetry in the large deviation functional for stochastic dynamics. J. Stat. Phys. 95, 333–365 (1999).
[25] C. Maes, The fluctuation theorem as a Gibbs property. J. Stat. Phys. 95, 367–392 (1999).
[26] J.R. Norris, Markov chains. Cambdrige University Press, Cambridge (1997).
[27] A. Parmeggiani, F. Jülicher, A. Ajdari, J. Prost, Energy transduction of isothermal ratchets: generic aspects and specific examples close to and far from equilibrium. Phys. Rev. E 60, 2127 (1999).
[28] P. Reimann, Brownian motors: noisy transport far from equilibrium. Phys. Rep. 361, 57–265 (2002).
[29] F. Ritort, Single-molecule experiments in biological physics: methods and applications. Journal of Physics C (Condensed Matter) 18, R531-R583 (2006).
[30] J. Schnakenberg, Network theory of microscopic and macroscopic behavior of master equation systems. Rev. Mod. Phys. 48, 571–585 (1976).
[31] J. Xing, H. Wang, G. Oster, From continuum Fokker–Planck models to discrete kinetic models. Biophysical Journal 89, 1551–1563 (2005).
[32] S.R.S. Varadhan, Large deviations and applications. CBMS-NSF regional conference series in Applied Mathematics 46. Society for Industrial and Applied Mathematics, Philadelphia 1984.

Alessandra Faggionato, Dipartimento di Matematica, Università di Roma “La Sapienza”, P.le Aldo Moro 2, 00185 Roma, Italy
E-mail address: faggioni@mat.uniroma1.it

Daniele Di Pietro, Dipartimento di Fisica, Università di Roma “La Sapienza”, P.le Aldo Moro 2, 00185 Roma, Italy