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Universal bound on the efficiency of molecular motors

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Abstract. The thermodynamic uncertainty relation provides an inequality relating any mean current, the associated dispersion and the entropy production rate for arbitrary non-equilibrium steady states. Applying it here to a general model of a molecular motor running against an external force or torque, we show that the thermodynamic efficiency of such motors is universally bounded by an expression involving only experimentally accessible quantities. For motors pulling cargo through a viscous fluid, a universal bound for the corresponding Stokes efficiency follows as a variant. A similar result holds if mechanical force is used to synthesize molecules of high chemical potential. Crucially, no knowledge of the detailed underlying mechano-chemical mechanism is required for applying these bounds.

Keywords: molecular motors

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1. Introduction

Molecular motors are small machines that can transform free energy liberated in a chemical reaction into mechanical work. Their thermodynamic efficiency η is defined as the ratio between the work exerted against an opposing mechanical force f (or torque for a rotary motor) and the free energy consumed in the chemical reaction driving the motor. This efficiency is universally constrained through the second law by one [1–17]. Molecular motors are isothermal machines for which $\eta \leq 1$ replaces the Carnot expression applicable to heat engines [18].

A thermodynamic uncertainty relation for non-equilibrium steady states has recently been obtained in [19] (see [20] for a rigorous proof). This relation involves the rate of entropy production, the average of any fluctuating current and the dispersion associated with this current. It is expressed as an inequality, which, *inter alia*, establishes the minimal thermodynamic cost of precision in biochemical processes like enzymatic reactions [21, 22]. Likewise, it can be used to infer unknown enzymatic schemes from measuring fluctuations of product formation in the spirit of statistical kinetics [23] and thermodynamic inference [24, 25]. Recently, it has been cast in the form of a design principle for non-equilibrium self-assembly [26], and it provides an alternative method to obtain a lower bound on the entropy production, as compared to the method from [27, 28]. As an important generalization of this uncertainty relation, bounds on the whole spectrum of fluctuations of such fluctuating currents have been derived [20, 29–32].

For the simple paradigmatic case of a driven system moving with time t along a coordinate x , the uncertainty relation reads [19]

$$\sigma \frac{D}{v^2} > k_B, \quad (1)$$

where k_B is Boltzmann's constant, σ the entropy production rate, v the mean velocity, and D the diffusion coefficient

$$D \equiv \lim_{t \rightarrow \infty} \langle (\Delta x(t) - \langle \Delta x(t) \rangle)^2 \rangle / 2t, \quad (2)$$

with $\langle \dots \rangle$ denoting steady state averages throughout. From a physical perspective, this relation shows that high precision, i.e. a small dispersion (or uncertainty), comes at the cost of high entropy production, i.e. dissipation.

In this contribution, we discuss the consequences of this thermodynamic uncertainty relation for the efficiency of molecular motors. As a main result, we show that η is bounded by

$$\eta \leq \frac{1}{1 + vk_B T / Df}, \quad (3)$$

where v is the (mean) velocity of the motor, D its diffusion coefficient, and T is the temperature. The intriguing aspect of this bound arises from the fact that v , D , and f are experimentally accessible quantities. No knowledge of the underlying chemical reactions scheme is necessary for applying this bound. Moreover, it holds for a huge class of motor models, arguably essentially for all models that are thermodynamically consistent whether based on discrete states or on a continuous potential as often used in ratchet models [2, 3, 33]. Likewise, it holds for complexes of motors pulling cooperatively a single cargo particle as, e.g. investigated in [15, 34–36].

2. Thermodynamically consistent motor model

The molecular motor (complex) has an arbitrary number of internal states $\{i\}$ that describe distinct conformations. Moreover, a possible change in conformation can be related to the binding of a solute molecule A^α . Here, α label the species, like ATP whose hydrolyzation to ADP and P_i can drive the motor. The motor steps along a periodic track of periodicity d , which means that the set of states $\{i\}$, called a ‘cell’, is attached to a discrete linear sequence of spatial positions for the center of the motor, see figure 1 [37].

Transitions from state i to state j can occur within a cell, i.e. without net advancement of the motor or can be accompanied with a forward or a backward step. In the first case, we denote the rate by k_{ij} , in the two latter by w_{ij}^+ and w_{ij}^- , respectively. The transitions are microscopically reversible, which means that whenever $k_{ij} \neq 0$, k_{ji} cannot vanish either. Likewise, $w_{ij}^+ \neq 0$ implies $w_{ji}^- \neq 0$ and vice versa. However, there may be transitions within a cell, which do not occur with spatial motion, i.e. $w_{ij}^{+,-} = 0$ is allowed even if $k_{ij} \neq 0$ and vice versa.

Thermodynamic consistency imposes the following two constraints on the rates. First, for transitions within one periodicity cell,

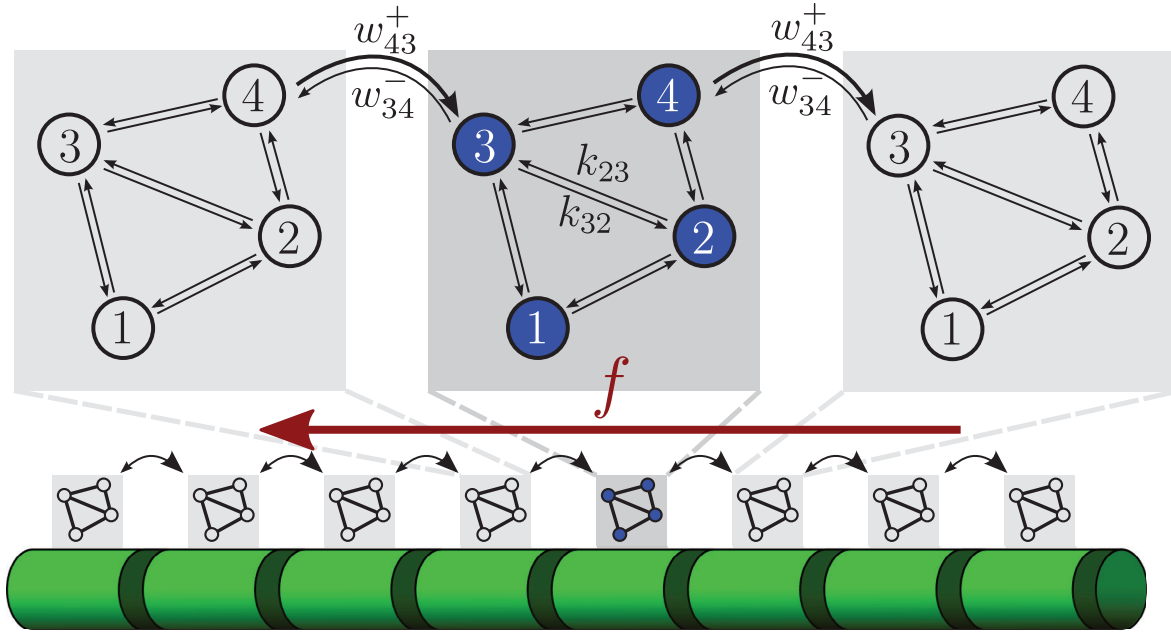


Figure 1. Schematic network of transitions for a molecular motor walking along a periodic track against an external force f . For each periodic interval the internal states $i \in \{1, 2, 3, 4\}$ of the motor can be grouped into a ‘cell’.

$$\frac{k_{ij}}{k_{ji}} = \exp \left[\left(F_i - F_j + \sum_{\alpha} b_{ij}^{\alpha} \mu^{\alpha} \right) / k_B T \right]. \quad (4)$$

Here, $F_{i,j}$ are the free energies of the two states, which may comprise contributions from the displacement against the external force for incomplete steps of the motor. If the transition from i to j requires binding a solute of species α (like, e.g. ATP), then $b_{ij}^{\alpha} = 1$. Likewise, if this transition leads to a release of such a molecule, $b_{ij}^{\alpha} = -1$. In both cases, the chemical potential μ^{α} of this species enters the expression in the exponent providing a contribution to the total free energy involved in such a transition. If a transition additionally involves a step in the forward direction, against the applied force, then the ratio between such a step and the corresponding backward step becomes

$$\frac{w_{ij}^+}{w_{ji}^-} = \exp \left[\left(F_i - F_j + \sum_{\alpha} b_{ij}^{\alpha} \mu^{\alpha} - fd \right) / k_B T \right]. \quad (5)$$

For a fixed applied external force f and externally maintained chemical potentials $\{\mu^{\alpha}\}$, the motor reaches a steady state with velocity

$$v = \sum_{ij} p_i (w_{ij}^+ - w_{ij}^-) d \quad (6)$$

with p_i the steady state probability to find the motor in the internal state i . This velocity

$$v = \langle \Delta x(t) \rangle / t = \langle n^+(t) - n^-(t) \rangle d / t \quad (7)$$

is given by the steady state average of the stochastic displacement $\Delta x(t)$, where $n^{+,-}(t)$ are the number of forward and backward steps along the track in time t . In order to apply the thermodynamic uncertainty relation, besides the diffusion coefficient D of the motor, as defined in equation (2), we need the rate of thermodynamic entropy production σ . Applying the general principles of stochastic thermodynamics to this model [18], it is given by

$$\sigma = k_B \sum_{ij} p_i \left(k_{ij} \ln \frac{k_{ij}}{k_{ji}} + w_{ij}^+ \ln \frac{w_{ij}^+}{w_{ji}^-} + w_{ij}^- \ln \frac{w_{ij}^-}{w_{ji}^+} \right). \quad (8)$$

Using the thermodynamic constraints (4) and (5), the steady state condition

$$\sum_j p_i (k_{ij} + w_{ij}^+ + w_{ij}^-) = \sum_j p_j (k_{ji} + w_{ji}^- + w_{ji}^+), \quad (9)$$

and the symmetry $b_{ij}^\alpha = -b_{ji}^\alpha$ leads to the expression

$$\sigma = \sum_{ij} p_i (k_{ij} + w_{ij}^+ + w_{ij}^-) \sum_{\alpha} b_{ij}^\alpha \mu^\alpha / T - f v / T. \quad (10)$$

The chemical work put into the motor arises from reactions of the type

$$\sum_{\alpha} r_{\nu}^{\alpha} A^{\alpha} \rightleftharpoons \sum_{\alpha} s_{\nu}^{\alpha} A^{\alpha}, \quad (11)$$

where $r_{\nu}^{\alpha} = 1$ if species α is an educt of the forward reaction of type ν and $s_{\nu}^{\alpha} = 1$ if species α is a product of this reaction. In the simplest case of just ATP hydrolysis, as for F₁-ATPase [1, 10, 12, 16] or kinesin [8, 38, 39], we have only one net reaction



In general, the rate of consumption of species α is given by

$$\rho_{\alpha} = \sum_{\nu} \gamma_{\nu} (r_{\nu}^{\alpha} - s_{\nu}^{\alpha}), \quad (13)$$

where γ_{ν} is the effective net rate of the reaction of type ν with $\gamma_{\nu} < 0$ if the reaction goes backward on average. Likewise, $\rho_{\alpha} < 0$ if, on average, species α is rather produced than consumed. Since we assume that all reactions are catalyzed by the motor acting as an enzyme, thus requiring binding and release as introduced above, this net rate can also be written as

$$\rho_{\alpha} = \sum_{ij} p_i (k_{ij} + w_{ij}^+ + w_{ij}^-) b_{ij}^{\alpha}. \quad (14)$$

The rate of consumption of chemical (free) energy, i.e. the rate with which chemical work is put into the motor, becomes

$$\dot{w}_{\text{chem}} = \sum_{\alpha} \rho_{\alpha} \mu_{\alpha}. \quad (15)$$

Inserting these expressions into the entropy production rate (10), we get

$$\sigma = (\dot{w}_{\text{chem}} - f v) / T = f v (1/\eta - 1) / T \quad (16)$$

with the thermodynamic efficiency [2]

$$\eta \equiv fv/\dot{w}_{\text{chem}} = fv/(fv + T\sigma). \quad (17)$$

3. The bound

Inserting the uncertainty relation (1) in (17), we obtain our main result stated in the introduction, copied here for convenience as

$$\eta \leq \frac{1}{1 + vk_{\text{B}}T/Df}. \quad (18)$$

Remarkably, this universal bound has been derived without any assumptions about the specific molecular mechanism driving the motor. It holds for a single motor as well as for complexes of several motors pulling a cargo to which an external force is applied. Hence, it is sufficient to measure the velocity and the diffusion constant of the motor to bound its thermodynamic efficiency. This bound can also be written in terms of the often used randomness parameter $r \equiv 2D/vd$ [5, 23, 38, 40]. With this quantity, the universal bound on efficiency (18) reads

$$\eta \leq \frac{r}{r + 2k_{\text{B}}T/fd}. \quad (19)$$

If only one type of chemical reaction, e.g. ATP hydrolysis is involved, the rate of chemical work becomes $\dot{w}_{\text{chem}} = \rho_{\text{ATP}}\Delta\mu$, where $\Delta\mu \equiv \mu_{\text{ATP}} - \mu_{\text{ADP}} - \mu_{\text{P}_i}$. The rate of ATP-consumption can then be bounded as

$$\rho_{\text{ATP}} \geq \left(f + \frac{vk_{\text{B}}T}{D} \right) \frac{v}{\Delta\mu}. \quad (20)$$

This relation makes it possible to infer the minimal rate of ATP consumption by measuring the first and second moments of the displacement of the motor.

4. Variants

So far, we have focused on the thermodynamic efficiency η where the motor runs against an external load. For motors pulling cargo through a viscous environment with no further external load, often the Stokes efficiency

$$\eta_{\text{S}} \equiv \gamma^{(0)}v^2/\dot{w}_{\text{chem}} \quad (21)$$

is used [33]. It compares the chemical work spent to the (mechanical) power required by a fictitious force to pull the cargo with a bare friction coefficient $\gamma^{(0)}$ at the same velocity through the viscous medium. Using $\sigma = \dot{w}_{\text{chem}}/T$ in the uncertainty relation (1), one easily gets

$$\eta_S \leq \gamma^{(0)} D / k_B T = D / D^{(0)}, \quad (22)$$

where the second equality follows from the Einstein relation between the bare friction coefficient and the bare diffusion coefficient $D^{(0)} = k_B T / \gamma^{(0)}$ of the cargo. Hence the Stokes efficiency is universally constrained by the ratio between the full diffusion coefficient of the motor cargo complex and the bare diffusion coefficient of the cargo. Again, this bound holds independently of all molecular details.

So far, we have assumed that the motor can be described by a set of internal states replicated along a spatially periodic track using a discrete master equation dynamics. For motors modeled in a continuous potential possibly changing due to internal (chemical) transitions [2] and for motors pulling big probe particles described by a Langevin equation [13, 41], these universal results remain valid. Formally, one has to discretize the spatial coordinate and introduce (biased) transition rates between neighboring spatial positions. After such a discretization, which can become arbitrarily fine, one is back at the model investigated above.

For a motor that performs chemical work $\dot{w}_{\text{chem}}^{\text{out}} > 0$ by synthesizing molecules with high chemical potential driven by an applied external force $f^{\text{dr}} > 0$ [42] similar results hold with velocity $v > 0$. The efficiency for this situation reads

$$\eta \equiv \dot{w}_{\text{chem}}^{\text{out}} / f^{\text{dr}} v = (f^{\text{dr}} v - T\sigma) / f^{\text{dr}} v \geq 0. \quad (23)$$

The inequality (1) leads to

$$\eta \leq 1 - v k_B T / f^{\text{dr}} D. \quad (24)$$

Again, the efficiency of this molecular machine can be bounded without measuring the rate at which it produces molecules.

5. Numerical case study

We illustrate the bound for a simple model of the rotary motor F₁-ATPase coupled elastically to a colloidal probe particle [13, 43]. As shown in figure 2(a), after mapping the rotary motion to a linear one, the motor performs discrete steps of length d , with each forward step hydrolyzing an ATP molecule and each backward step synthesizing an ATP molecule. The stepping rates depend on the chemical potential difference $\Delta\mu$ of the ATP reaction and the elongation of the linker to the probe particle. The continuous dynamics of the probe particle with friction coefficient $\gamma^{(0)}$ is modeled as overdamped Brownian motion subject to the external force f and the potential force of the linker [13].

The average velocity v and the diffusion constant D for this model can be calculated numerically from the master equation that is obtained by finely discretizing the possible elongations of the linker and truncating at large elongations. Due to the tight coupling between the chemical reaction and the motion of the motor, the rate of the chemical work is $\dot{w}_{\text{chem}} = \Delta\mu v / d$ [13], so that the thermodynamic efficiency (17) becomes trivially

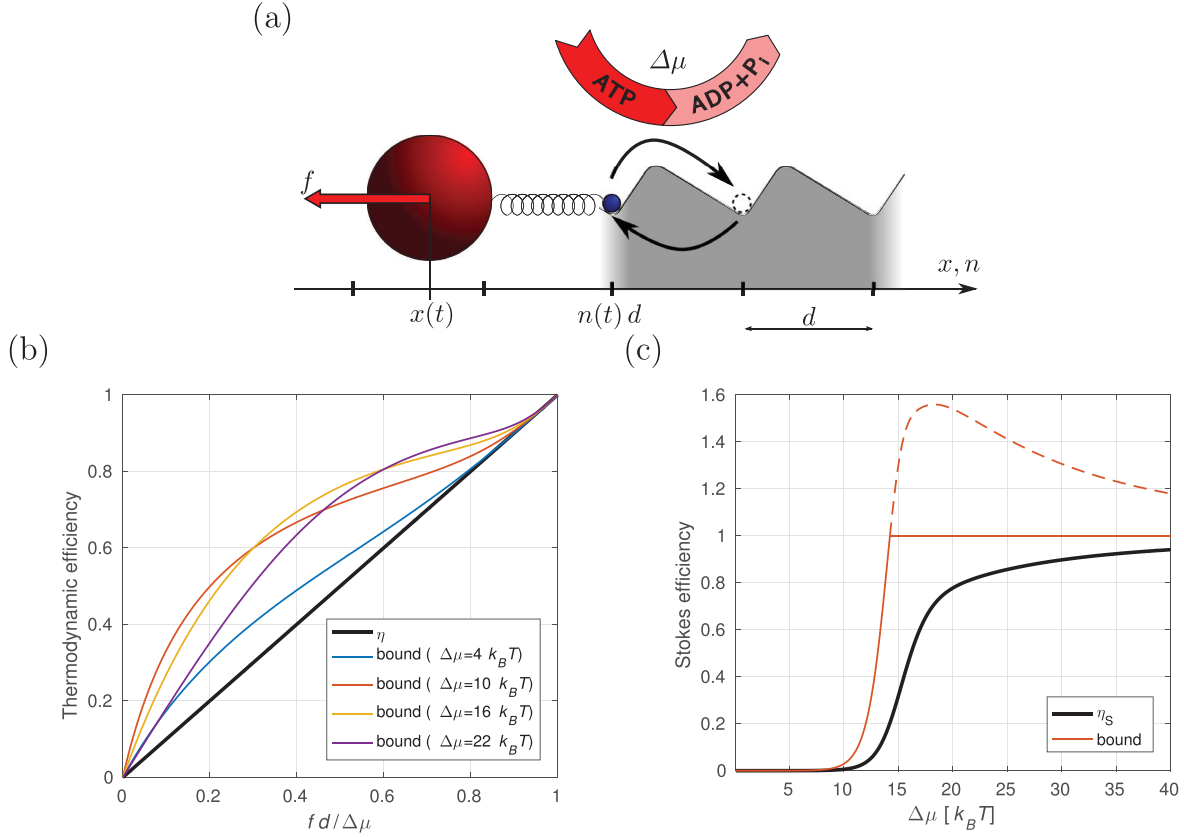


Figure 2. (a) Illustration of the model for an ATP driven motor (blue) elastically coupled to a probe particle (red), to which the external force f is applied. (b) Comparison of the thermodynamic efficiency η as a function of the scaled force $fd/\Delta\mu$ (black line) and the bound (18) at various values of $\Delta\mu$ (colored curves). (c) Comparison of the Stokes efficiency as a function of $\Delta\mu$ (black) and the bound (22) (red). For large $\Delta\mu$, where the bound surpasses 1, it is continued as a dashed line. Model parameters were chosen as detailed in [13], different values of $\Delta\mu$ were generated by varying the concentration of ATP while keeping the concentrations of ADP and P_i fixed.

$$\eta = fd/\Delta\mu \quad (25)$$

while the Stokes efficiency (21) is

$$\eta_s = \gamma^{(0)}vd/\Delta\mu. \quad (26)$$

In figure 2(b), we compare the thermodynamic efficiency (25) to the bound (18) for forces ranging from 0 to $\Delta\mu/d$ and selected values of $\Delta\mu$. The bound is trivially saturated for $f=0$ and for the case $fd = \Delta\mu$, where the chemical and the mechanical force balance each other, leading effectively to equilibrium conditions with vanishing velocity. Since the uncertainty relation becomes exact within linear response for unicyclic systems [19, 20], the bound is also saturated for forces close to $\Delta\mu/d$. Similarly, for $\Delta\mu \rightarrow 0$, the bound approaches η for all $0 < f < \Delta\mu/d$.

In figure 2(c), the Stokes efficiency (26) is compared to the bound (22) for a range of $\Delta\mu$ and constant $f=0$. While this bound is also saturated in the linear response regime

for $\Delta\mu \rightarrow 0$, it becomes rather loose for large values of $\Delta\mu$. It even surpasses the bound $\eta_S < 1$, proven in [33], when D becomes larger than the bare diffusion coefficient $D^{(0)}$ [44, 45]. Obviously, the bound (22) is not useful in this range of parameters.

6. Conclusion

We have derived a universal bound on the efficiency of molecular motors that depends only on the fluctuating displacement of the motor. The sole knowledge of both the average and the dispersion of this experimentally accessible quantity yields a bound that is independent of the underlying mechano-chemical reaction scheme. This result applies to any nano or micro machine operating in an environment of fixed temperature. Extensions to devices coupled to two heat baths of different temperature should be possible and are left for future research.

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