THE EFFICIENCY OF ENERGY CONVERSION FOR AN ENTROPY DRIVEN STEPPER MOTOR WALKING HAND-OVER-HAND*

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Molecular engines are nano-scale machines operating under far-from-equilibrium conditions. In living cells they transform chemical energy into mechanical work while acting under randomly fluctuating forces in the form of thermal noise. In this paper we discuss a previously introduced model of a stepper motor [M. Żabicki, E. Gudowska-Nowak, W. Ebeling, *Chem. Phys.* in press], which is able to drive the system uphill at the cost of the energy inflow from an energy reservoir. The efficiency of the motor is defined as the ratio of the power exerted in the uphill motion with respect to the energy influx from the depot. We analyze the efficiency of this system by adapting the motor model in which only the internal motion includes inertia, whereas the motion of its center of mass becomes overdamped. Based on the numerical simulations of the center of mass trajectories and analysis of directed fluxes of motor particles moving along a one-dimensional track, we derive thermodynamic estimates of the motor efficiency as a function of the opposing force.

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1. Introduction

The great challenge in the field of nanotechnology is nowadays the design and construction of microscopic synthetic motors that could transform externally supplied energy into a programmed motion and perform dedicated

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mechanical tasks such as *e.g.* pumping of matter or charges and transporting a cargo [1,2]. In nature many cellular processes require nano-scale molecular motors to produce motion and forces [3,4]. Those molecular devices are proteins that are capable to convert chemical energy from the hydrolysis of ATP into mechanical work used to power *e.g.* intracellular transport of organelles. Valuable insights into the chemomechanical energy transduction by protein motors has been achieved over the past 10 years thanks to the technical developments that allow detection and manipulation of motor proteins at a single molecule level [3,5]. Additionally, solving the atomic structures of protein motors and building atomic models of actin filaments and microtubule have improved understanding of motor motility along their tracks [5–7]. The results coming from the structural analysis and single-molecule experiments support [8, 9] the concept of protein motors as nano-machines built up of levers, springs and swivels synchronized in a coordinated action.

Theories describing motility of molecular motors comprise various levels of complexity starting from simple kinetic models [10, 11] with few states to all atom molecular dynamics [12]. Novel computational approaches to kinematics of molecular motors are based on coarse-grained structural models in which pre-defined groups of atoms form a system of semi-rigid bodies connected by joints [12,13]. Whereas contacts between the clusters of atoms enforce excluded volume constraints, the spring-like potentials model system elasticity and provide a simple representation for conformational changes of motors. Formation and rupture of adhesive bonds between individual molecules which gives rise to the protein friction [14] is also an important ingredient of molecular simulations.

Unlike macroscopic motors, motor proteins operate in "low Reynolds number environments" [3, 15, 16]. Viscous forces (dependent on particle dimensions) dampen the motion and dissipate kinetic energy so that the motor has to be provided with a specific energy to move and to perform its tasks. In a macroscopic machine, this energy supply is often provided through a directional force when work is done to move mechanical components in a particular way. As moving bodies become less massive and smaller in dimensions, inertial terms decrease in importance and viscosity begins to dominate. Accordingly, a common approach in physical modeling of molecular motors is based on the paradigm of an overdamped Brownian particle undergoing a random walk in a periodic, asymmetric potential representing the surface of the track [13] and subject to additional, external (possibly time-dependent) forces. Observation of a preferential direction of motion in such a system is possible if the time-inversion symmetry is broken (often, this condition is colloquially stated as "breaking of the detailed balance symmetry" [16, 17]).

In this paper we analyze efficiency of a stepper machine [18], which is based on a previously developed ratchet motor model with an energy depot [19–21]. The stepper motor is mimicking hand-over-hand mechanism of the kinesin motion [22]. We follow description of the stepping as proposed by Bier [16] and derive a model of a thermodynamic machine [23] which reflects basic characteristics of the Carnot cycle [18]. An essential element in our model is the expansion and contraction of a polymer linker connecting two units (heads) of the kinesin dimer, each of which consists of about 350 amino acids. When kinesin moves on a microtubule surface, it performs steps of amplitude 8.1 nm, the distance between adjacent tubulin sites [3]. The steps are powered by the hydrolysis of ATP and each step involves consumption of about one ATP molecule with a release of energy of about $13\,k_{\mathrm{B}}T$. The idealized kinesin stepper motor starts its motion in a state of high energy and low entropy [11] with a linker band stretched between its heads. Performing the motion requires the head to be first detached what causes loosening of the linking band and increases entropy.

After separation of relative motion of heads and center-of-mass motion of the whole kinesin, the kinematics of the center of mass of the motor can be described by an overdamped Langevin equation. In contrast, the inertia plays an important role in the relative motion of the heads [18]. Here, we investigate the average velocity of the motor by simulating exemplary trajectories of motion and analyzing their ensemble properties.

2. Molecular Motor Model and its directional motion

We adopt a modeling approach at the level of a Brownian ratchet, assuming that the motor is restricted to moving in one spatial dimension along a biopolymer track of a tubulin and is subjected to random bombardments of surrounding fluid molecules. The motor itself consists of two similar units (heads) connected by a rubber-like linker. After detachment of the head from the trail, the linker band relaxes and its coiling increases the entropy of the system. The docking of the head in the next binding site of the potential is followed by an expansion of the polymer and a decrease of entropy. The stepping mechanism is powered by the energy supply from the external depot which is permanently filled with the chemical energy of the ATP hydrolysis and absorption [11, 18].

We consider first the stochastic motion of kinesin heads governed by the Langevin equation:

$$\frac{mdv(t)}{dt} + m\gamma_0 v(t) + \left(U_1'\left(x_{\mathrm{c}} + \frac{x(t)}{2}\right) - U_1'\left(x_{\mathrm{c}} - \frac{x(t)}{2}\right)\right) - 2TS'(x(t))$$
$$= mde(t)v(t) + m\sqrt{2D_v}\xi(t)\,, \tag{1}$$

where $U(x)$ is a ratchet-type potential representing the surface of the microtubule with docking locations for the stepper, γ_0 is a friction frequency acting on the relative motion of the heads, $x(t) = x_1(t) - x_2(t)$ and $v(t) = v_1(t) - v_2(t)$ are relative position and speed of kinesin heads (labeled 1, 2 respectively). The coordinate $x_c = (x_1(t) + x_2(t))/2$ stands for the center of mass position[1] and $\xi(t)$ represents the white Gaussian noise of intensity $m\sqrt{2D_v}$ with $D_v = \gamma_0 k_B T/m$. The term $TS'(x)$ denotes entropic force exerted by an extended elastomer linking kinesin heads. As the length of the elastomeric band decreases, the entropy of the system increases by ΔS. Note that for an ideal stretched elastomer the decrease in length corresponds to an increase of volume of an ideal gas. The first law of thermodynamics can be then written as $dE = TdS + F_S dx$ with an equation of state $F_S = k_B T f(x/x^*)$, where x^* is the contour length in a worm-like-chain model for an unstructured polypeptide [4]. Up to the first approximation, the entropic force is nearly constant for a small end-to-end distance of a linker and strongly increases, *i.e.* deviates from linearity at larger extensions of the polymer [14]. As discussed elsewhere [14], deviations from the linearity can be also induced at small end-to-end distances conditioned on the properties of the solvent and molecular crowding. For the purpose of modeling we have adopted an analytic form of the entropy with a flat central region incorporating two small maxima:

$$TS(x) = s_0 + ax^2 - bx^4\,, \tag{2}$$

hence the force $F_S = TS'(x) = 2x(a - 2bx^2)$ is nonlinear. It should be stressed, however, that additional tests performed on the model with alternative forms of the rubber band potential (like *e.g.* piece-wise linear) showed that our results are insensitive to the details of the entropy model.

The mechanical energy of motion is powered by the energy flow $de(t)/dt$ from the depot (reservoir) which depends on the coupling d between the motor and the energy reservoir. The energy accumulated in the depot container q can be dissipated with a rate c. Altogether, the corresponding dynamics for the energy reads

$$\frac{de(t)}{dt} = q - ce(t) - mdv^2 e(t)\,. \tag{3}$$

The equation of motion of the center of mass may be written as [18]

$$\frac{dx_c(t)}{dt} = \frac{F_0}{\Gamma} - \frac{1}{\Gamma}\left[U_1'\left(x_c + \frac{x(t)}{2}\right) + U_1'\left(x_c - \frac{x(t)}{2}\right)\right] + \sqrt{2D_{x_c}}\xi_0\,, \tag{4}$$

[1] Note, that for a separate head, the equation of motion reads $m\ddot{x}_i = -m\gamma_0\dot{x}_i - U'(x_i) + F_S(x_1 - x_2) + mde(t)\dot{x}_i - M\Gamma_0\dot{x}_0 + m\sqrt{2D_v}\xi_i$.

where F_0 is an external force acting at the center of mass and Γ is the center of mass friction. We note that the term in the parenthesis models the force exerted on the center of mass, generated by the relative oscillatory motion of two heads. In the above formulation the mass and friction of the complex system are not simple (additive) functions of two masses and two friction coefficients representative for the motion of heads [18]. Considering that $x(t)$ is a periodic function of time [18], the overdamped dynamics in the center-of-mass resembles clearly resembles the scenario of flashing ratchets [13, 24, 25] in which an intriguing phenomenon of a negative mobility has been observed.

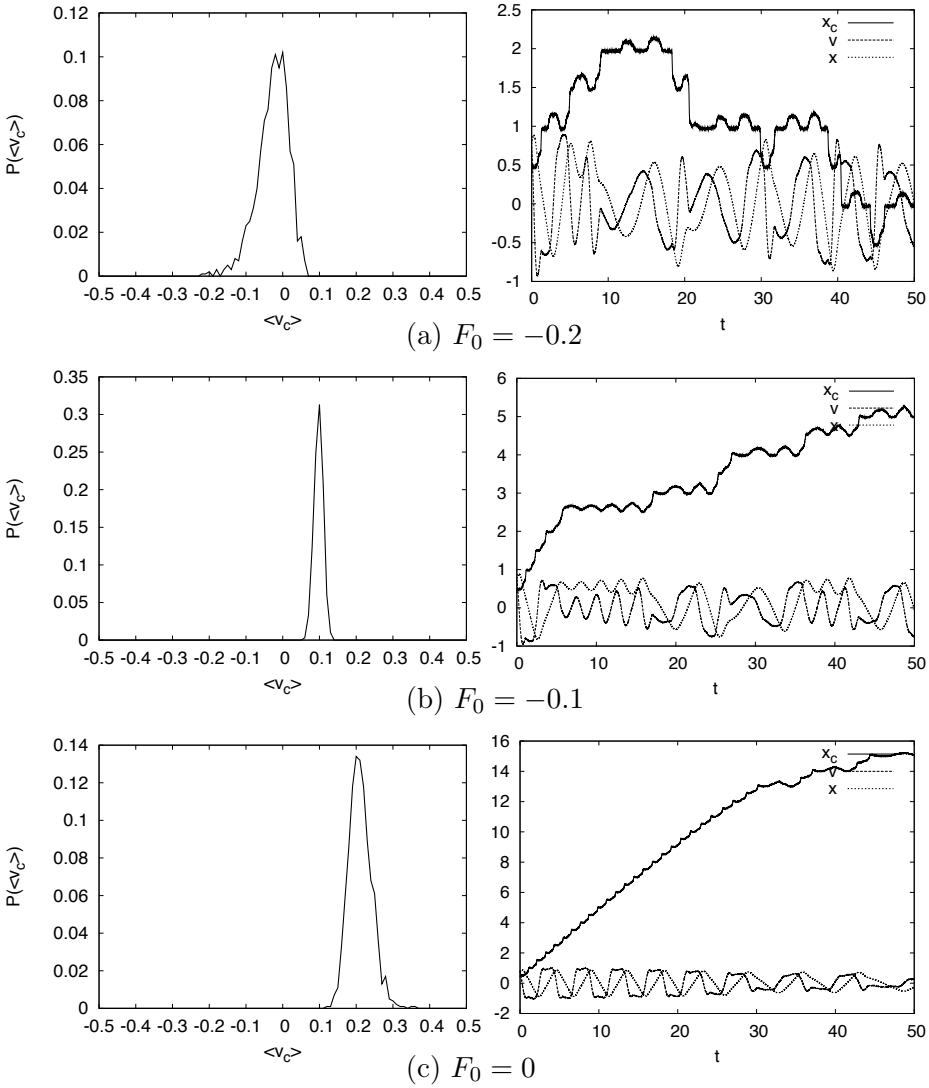
For the ratchet potential $U(x)$ we use the standard model [26]

$$\begin{aligned} \frac{U(x)}{E_0} &= -F_0 x + U_1(x)\,, \\ U_1(x) &= h\left[0.499 - 0.453(\sin(2\pi(x+0.1903)) + \tfrac{1}{4}(\sin(2\pi(x+0.1903)))\right]\,, \end{aligned} \tag{5}$$

where F_0 is an external biasing force directed to the left and h is the height (amplitude) of the barriers (in relation to E_0). The above set of equations has served as a prototype of an entropy-driven stepper model. The results of numerical simulations of Eqs. (1), (3), (4) are discussed in the next section.

3. Simulations of motor trajectories

Results discussed in this paragraph have been derived from model trajectories simulated for a constant set of parameters, *i.e.*: $\gamma_0 = 0.02$, $m = 1$, $D_v = 0.1$, $q = 1$, $c = 0.1$, $d = 0.960061$, with initial values $v_0 = 0.745513$, $x_0 = 0.771748$, $e_0 = 0.023095$. The parameters of the entropy model have been fixed to $a = 0.5$ and $b = 1.0$, respectively. The discrete time step has been set to $\Delta t = 10^{-3}$ and integration of the equations of motion has been performed up to the final time $t_{\rm fin} = 50.0$. At each time step, the relevant velocities of the center-of-mass motion have been recorded and finally averaged over the time $\langle v_c \rangle = 1/t_{\rm fin} \int_0^{t_{\rm fin}} dt v_c(t)$. Data obtained have been further averaged over 10^5 trajectories. The left panel of Fig. 1 depicts normalized frequency histograms estimating (long time) probability density function $P(\langle v_c \rangle)$. We note that for a special choice of parameters our dynamic system might possess several attractors [20]. Accordingly, the initial conditions for the simulations have been chosen to assure that trajectories start in the basin of the "uphill attractor". This guarantees that the system is able to convert the (chemical) energy extracted from the depot into the mechanical work used to move the stepper system uphill the potential and against the biasing force F_0.



(a) $F_0 = -0.2$

(b) $F_0 = -0.1$

(c) $F_0 = 0$

Fig. 1. Mean velocity distribution as a function of the load F_0 (left panel), with sample trajectories of the motion depicted in the right panel. The friction for the center-of-mass motion has been set to $\Gamma = 0.101790$. Histograms of the time-averaged velocity $\langle v_c \rangle$ have been obtained for 10^5 trajectories, each of which had duration $t_{\mathrm{fin}} = 50$.

The exemplary trajectories of the stepper motion are presented in Fig. 1. Note that the biasing force F_0 which models the load is negative, *i.e.* it is pointing to the left. In contrast, in almost 100% cases, the motor consumes the energy and performs the motion in an opposite direction, *i.e.* it moves uphill against the force F_0.

The efficiency of performing that work at the cost of energy extracted from the depot has been further determined by use of the formula [27]

$$\eta = \frac{|F_0|\,\langle\langle v_c\rangle\rangle}{q}\,, \tag{6}$$

with $\langle\langle v_c\rangle\rangle$ being the ensemble average of the (long time) velocity v_c:

$$\langle\langle v_c\rangle\rangle = \int_{-\infty}^{\infty} P(\langle v_c\rangle) d\,\langle v_c\rangle\ . \tag{7}$$

The above expression has been used to derive functional dependence of η on the load F_0, *cf.* Fig. 2. Closer inspection of Fig. 1 indicates, that for a given set of parameters, the average velocity $\langle\langle v_c\rangle\rangle$ depends on the load F_0 and approaches zero for a stalling force $F_0 = -0.2$. The profile of the efficiency of energy conversion $\eta(F_0)$ (*cf.* Fig. 2) corresponds to a non-monotonous function of the load and varies between the stalling force and the vanishing bias $F_0 = 0$. For values $F_0 \in (-0.2; 0)$, the motor steps uphill (to the right). Its efficiency η assumes a maximum value of about 12% for $F_0 = -0.18$ and acquires vanishing values at $F_0 = -0.2$ (the average velocity drops to zero) and at $F_0 = 0$, (the work performed by the motor vanishes). The bell-like shape of the energetic efficiency reflects the changes in the average velocity of the stepper and assumes the form similar to the experimentally observed efficiency of kinesins [22, 27].

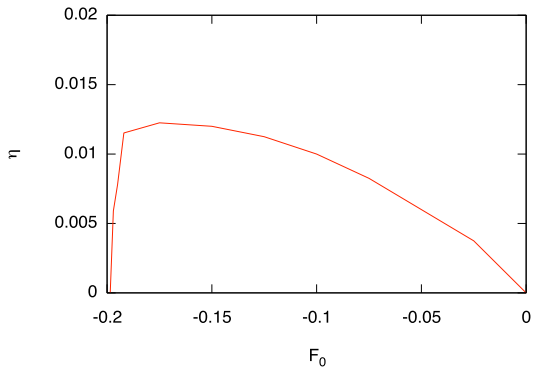


Fig. 2. Efficiency as a function of the force F_0. $\Gamma = 0.101790$.

4. Conclusions

We have analyzed kinematics of a stepper motor driven by the energy supply from an external depot. The energy of the reservoir constantly changes in time: the inflow of (chemical) energy to the depot competes with its dissipation and conversion to the mechanical energy of the motor. The two-head stepper is assisted by a nonlinear entropic force acting between its units. We have documented that (for appropriate parameters and initial conditions) such a primitive model device is able to transform the depot energy to perform work against the external force (load) in the uphill motion. The efficiency of energy transduction displays the typical behavior observed in experiments with molecular motors [22, 27]. The function first increases with the (negative) load force and then abruptly drops to zero. The maximal value of η as observed for the special parameter set in our simulations reached about 10–15 percent. The losses in performance of the motor are due to the dissipative mechanisms in the depot and the mechanical friction acting on the stepper. At the critical (stalling) load force the motor stops to operate. More detailed studies of the influence of the loss factors and the entropic force on different efficiency measures will be presented elsewhere.

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