Modeling and Role of Feedback Controlled Stochastic Ratchets in Cellular Transport

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Abstract— This paper develops a model for Brownian ratchets to analyze the cases where the transport characteristics are affected by feedback mechanisms. One main application of this approach is to gain insights on the intracellular transport of motor proteins (such as Kinesin and Dynein) on a microtubular track, and on the role of feedback control on their transport. The model comprises of a stochastic system where the system switches between two stochastic differential systems, where the switching criteria is a state-dependent stochastic variable. Simulations demonstrate that the feedback mechanism helps achieve an increased average velocity of transport and corroborates the hypothesis that a motor protein can achieve higher speeds of transport by restricting or enabling attachment/detachment of ATP/ADP like molecules depending on conformational changes in the motor-protein.

Keywords: Brownian ratchets, kinesin walk, cellular transport, Kolmogorov-Chapman differential equations, stochastic differential equations, switched/hybrid systems

I. INTRODUCTION

Stochastic or Brownian ratchets include mechanisms that attempt extracting useful work from thermal noise. Extracting such work under equilibrium and isothermal conditions is impossible (it violates the second law of thermodynamics) even though for some mechanisms, at the first appearance, it seems plausible. Feynman in [7] postulates the need for non isothermal strategies to extract work from naturally occurring diffusive processes. In molecular systems, unlike macro-scale systems, maintaining thermal gradients as suggested in [7]

is challenging and often not possible due to their small length scales. Given this difficulty, employing thermal noise processes for useful purpose under isothermal conditions is possible with non-equilibrium strategies. In a *flashing ratchet,* a particle undergoing diffusive motion is subjected to a *flashing* potential where, a spatially periodic asymmetric potential is switched on and off in an alternating manner. It can be shown that such an asymmetric flashing potential can lead to preferential direction of motion for the particle when it is switched on and off.

Apart from the potential use of flashing ratchets in engineered systems, they are fundamental to certain models that explain how biological systems at the molecular scale use thermal noise effectively [2]. The potential impact of understanding and proper modelling of these cellular transport phenomena is immense since improper functioning of these processes are related to diseases such as Alzheimer's [9]. One such system that we focus on is the intracellular transport of cargo by motor proteins on microtubule tracks, which according to a hypothesis, is well explained by flashing-ratchet principle (see Figure 1).

Microtubules are polymers of tubulin subunits (dimers). Each such dimer unit can be considered a dipole unit. In this hypothesis, a microtubule track that consists of a periodic array of dimer units provides the periodic electrostatic spatial potential for the motor proteins that use these tracks. It is known that the motor proteins use ATP-ADP hydrolysis to execute motion on microtubule tracks. The acquisition of an ATP molecule leads to the motor molecule component interacting with the track that results in switching on the electrostatic potential. On the other hand the neutralization of the charge brought about by acquisition of ATP leads to the motor molecule component interacting with the track to feel no force. Also, the motor molecule is in a thermal bath and is thus subject to diffusion. Thus all the ingredients that constitute the flashing-ratchet mechanisms are present in the molecular motor based transport. We remark that the molecular motor instead
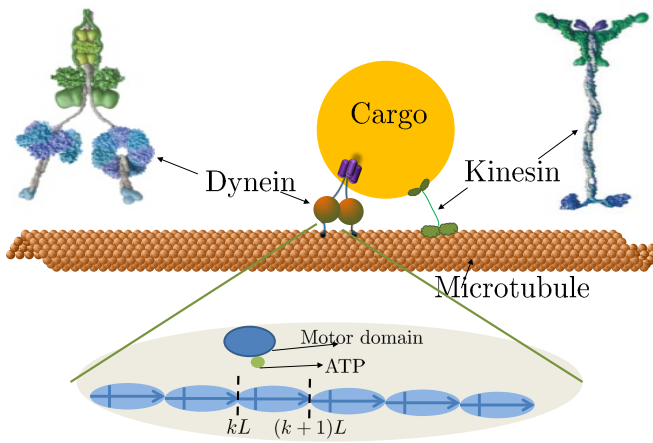
Fig. 1. Schematic showing the underlying brownian ratchet parametrs for motr transport.

of feeling no potential or the entire potential based on the ATP presence or absence, in all likelihood, feels a modulation of the forces. Here the molecular motor feels a smaller electrostatic force in the absence of ATP and a scaled up version (with the relative shape of the potential being the same) in the presence of ATP. This model constitutes our main motivation for analyzing Brownian-ratchet models and coming up with control strategies that modify their behavior, which potentially can provide remedial actions for defective cellular transport.

Over the last two decades, several models that study the ratchet mechanisms have been developed in the physics literature [1], [2], [10]. Feedback control of flashing ratchets for increasing transport velocity has already received attention in the literature [3], [4], [11]. Existing feedback strategies involve instantaneous switching of potential levels based on the particle position; in their strategies, when the particle is in a favorable position (i.e., the potential at that position will drive the particle forward), the potential is switched on and it is kept off otherwise. These switchings during the transitions of the particle from favorable to unfavorable positions and vice-versa are considered to be instantaneous [3], [4], or with a deterministic delay [5], [6]. These strategies are well suited for systems that allow high degree of control (actuation) authority. However, in the biological system described above, it is realistic to assume that the position and conformational change based intrinsic feedback may only change the rate of ATP acquisition and hence the switching rates; it can not make the potential switch instantaneously. This is the primary difference of our model from the existing models which makes it suitable for certain physical and

biological scenarios such as the cellular transport.

In this article we develop a model of Brownian ratchets that can be used to study such cases where intrinsic feedback changes the transport characteristics. In the model that we consider, the applied potential flashes between two levels (biased up and down), that corresponds to ATP acquisition and ADP dissociation. As the ATP acquisition is a random phenomenon, in our model the switchings are stochastic. The switching rate, however, is deterministic and may depend on many physical factors such as ATP concentration, the position of the motor head within a unit of the periodic lattice of the microtubule and the like. Such a position-dependent control of switching rate is possible in the molecular motors where conformational and steric hindrances regulate the ability of acquiring ATP molecules. To the best of the knowledge of the authors, such mechanisms have not received attention and might provide deeper insights into how the molecular motors execute diverse sets of transport related tasks. Also, this modeling can help identify modalities of transport mechanisms that the motor proteins engage in by delineating parameters that can be measured experimentally and can reflect on the various phases of transport. Mathematically, the underlying problem can be thought of as design of feedback control for a hybrid system, where the system switches between two *stochastic systems* described by corresponding stochastic differential equations, where the switching rate itself is also a stochastic parameter.

II. MODEL

Working Principle

In a typical flashing ratchet, a spatially periodic potential (see Figure 1) is switched on and off in an alternating manner for time intervals t_{on} and t_{off} respectively. An important and critical feature of this spatially periodic potential is its *asymmetric* shape within a spatial period, whereby the particle feels a force opposed to the desired direction of motion when its position is in the first $\alpha \neq \frac{1}{2}$ fraction of the period and feels a force in the desired direction of motion in the remaining $(1-\alpha)$ fraction of the period. Consider for example, the potential shown in Figure 2, that illustrates a potential with a steep positive slope (force being negative) in the interval $(kL, (k+\alpha)L]$ (with $\alpha < \frac{1}{2}$) of the kth spatial period. It can be shown that such an asymmetric potential can lead to preferential direction of motion for the particle when it is switched on and off. The basic principle why such motion can be achieved is as follows. Assume that the potential is
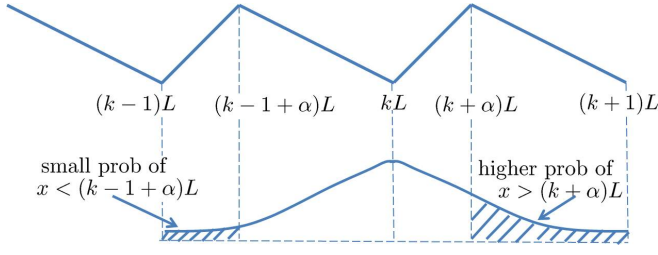
Fig. 2. Schematic showing the flashing ratchet parameter.

off in the time interval $[0, t_{off}]$, and the particle is at $x = 0$ at time $t = 0$. In this time interval, the particle motion is described by Brownian motion, that is, the probability density function of its position is described by

$$p(x, t|0, 0) = \frac{1}{\sqrt{4\pi t}} e^{\frac{-x^2}{4t}}, \tag{1}$$

whose mean is at $x = 0$ does not change with time, while the variance increases linearly with time t. The particle diffuses according to the above pdf for a time t_{off} at the end of which its pdf is described by (1) with $t = t_{off}$. Evidently the probability of finding the particle in the region $x > \alpha L$ and $x < -(1 - \alpha)L$ are given by $\int_{\alpha L}^{\infty} p(x, t|0, 0)dx$ and $\int_{-\infty}^{-(1-\alpha)L} p(x, t|0, 0)dx$ respectively. Noting that the length αL is smaller than the length $(1 - \alpha)L$, the probability of finding the particle (using (1)) in the region $x > \alpha L$ will be higher than the probability of finding the particle in the region $x < -(1 - \alpha)L$ at the time $t = t_{off}$. Now when the ratchet potential is turned on, there is a higher probability of finding the particle under the influence of a positive force, and if t_{on} is long enough, the particle will more likely settle in the well whose minimum is at $x = L$. In contrast the probability of finding the particle inside the well with a minimum at $-L$ will be considerably smaller. Thus on an average, the particle will move to the right. The above description provides the essence of the principle on which the flashing ratchets and their modifications operate. Note that it is evident that there will be no effective transport when the ratchet is kept on (or off) for all the time or when the ratchet potential is symmetric within a period (i.e. $\alpha = 1/2$).

Mathematical Model

In the following we model a flashing ratchet, where the particle is under the influence of white noise, that switches between two potentials, such that the corresponding drift (forces) exerted on the particle are different. We describe the position $x(t)$ of an inertialess particle under such a ratchet by the following two stochastic differential equations (SDE)

$$dx = f(x, \theta)dt + \sqrt{D}dW \tag{2}$$

where $\theta \in \{0, 1\}$, D is the Diffusion constant, and $W(t)$ is the Wiener process. The nondimesionalized potential $V(x, \theta)$, and therefore the corresponding force $f(x, \theta) = -\frac{\partial}{\partial x}V(x, \theta)$, acting on the particle switches (or flashes) between two functions, one defined for each θ ($\theta = 0$ or $\theta = 1$). The evolution of the switch-trigger parameter can be modeled to be deterministic with $\theta = 0$ for a duration t_{off} and on for a subsequent duration t_{on}, or can be modeled as a stochastic parameter. In this work, we assume a stochastic model for dynamics of θ where it has a certain switching rate. Thus the flashing ratchet model can be viewed as a stochastic hybrid system, where *both* the switch-trigger dynamics as well as individual system dynamics are stochastic.

In this paper we use the differential Chapman-Kolmogorov (DCK) equation [8] for modeling the transport of a particle under a flashing ratchet. In the DCK formulation, a partial differential equation is sought that describes the evolution of the probability density function $p(x, \theta, t|x_0, \theta_0, t_0)$, that is, it seeks the pdf of the random state (x, θ) at time t given that the state was (x_0, θ_0) at time t_0. Under fairly mild assumptions [8], this pde is completely determined by three functions - the drift $A(x, \theta, t)$, the diffusion $B(x, \theta, t)$, and the jump rates $Q(x, \theta|x_0, \theta_0, t)$ that we describe next.

A. Jump rate terms

The jump-rate from state (z, θ_0) to (x, θ) at time t is defined by (see [8])

$$Q(x, \theta|z, \theta_0, t) := \lim_{\Delta t \to 0} \frac{p(x, \theta, t + \Delta t|z, \theta_0, t)}{\Delta t} \tag{3}$$

under the assumptions that $|(x, \theta) - (z, \theta_0)| \geq \epsilon > 0$ and that the limit exists uniformly for all x, z, t and $\epsilon > 0$.

We assume that the position x of the particle is well behaved, that is, there is no instantaneous jump in the displacement of the particle when the ratchet flashes between two potentials. More specifically, we assume that as θ switches from 0 to 1,

$$\lim_{\Delta t \to 0} p(x, t + \Delta t|z, t, \theta(t) = 0, \theta(t + \Delta t) = 1) = \delta(x - z).$$

Furthermore we assume a model for switching dynamics from $\theta = 0$ to 1 given by

$$\lim_{\Delta t \to 0} \frac{1}{\Delta t} p(\theta(t + \Delta t) = 1|z, t, \theta(t) = 0) =: \lambda(z, 0).$$

Accordingly we have

$$Q(x, \theta = 1 | z, \theta_0 = 0, t) = \delta(x - z)\lambda(z, 0).$$

and,

$$Q(x, \theta = 0 | z, \theta_0 = 1, t) = \delta(x - z)\lambda(z, 1).$$

B. Drift terms

The drift terms given by $A_z(z, \theta, t)$ and $A_\theta(z, \theta, t)$ (see [8]) are respectively defined by

$$\lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_{\Omega_\epsilon} (x - z) p(x, \theta_0, t + \Delta t | z, \theta, t) dx d\theta_0$$

and

$$\lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_{\Omega_\epsilon} (\theta_0 - \theta) p(x, \theta_0, t + \Delta t | z, \theta, t) dx d\theta_0,$$

where

$$\Omega_\epsilon = \{(x, \theta) \text{ such that} |(x, \theta_0) - (z, \theta)| \le \epsilon\}.$$

Within the domain of integration, it is not possible for $\theta \ne \theta_0$ and thus we have $A_\theta = 0$ and $A_z(z, \theta, t) = f(z, \theta)$.

C. Diffusion terms

The diffusion terms are defined by $B_{zz}(z, \theta, t)$, $B_{\theta, z}(z, \theta, t)$ and $B_{\theta, \theta}(z, \theta, t)$, (see [8]) given by

$$\lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_{\Omega_\epsilon} (x - z)^2 p(x, \theta_0, t + \Delta t | z, \theta, t) dx d\theta_0,$$

$$\lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_{\Omega_\epsilon} (x - z)(\theta_0 - \theta)$$
$$\times p(x, \theta_0, t + \Delta t | z, \theta, t) dx d\theta_0,$$

and

$$\lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_{\Omega_\epsilon} (\theta_0 - \theta)^2 p(x, \theta_0, t + \Delta t | z, \theta, t) dx d\theta_0$$

respectively. As was the case for the drift term, it is not possible for $\theta \ne \theta_0$ within the domain of integration and thus $B_{\theta, \theta} = B_{\theta, z} = 0$ and $B_{zz}(z, \theta, t)$ evaluates to the constant D.

D. The differential Chapman-Kolmogorov Equation for Brownian ratchets

Substitution of the above computed quantities gives us a DCK of the following form :

$$\dot{p}(z, \theta, t | y, \theta_0, t_0) = -[f(z, \theta) p(z, \theta, t | y, \theta_0, t_0)]'$$
$$+ \frac{1}{2} D p''(z, \theta, t | y, \theta_0, t_0) \tag{4}$$
$$+ \lambda(z, 1 - \theta) p((z, 1 - \theta, t | y, \theta_0, t_0)$$
$$- \lambda(z, \theta) p(z, \theta, t | y, \theta_0, t_0).$$

Here $(\dot{\cdot})$ represents the partial derivative with respect to time, and $(\cdot)'$ and $(\cdot)''$ represent the first and second order partial derivatives with respect to the spatial variable.

III. FEEDBACK-BASED SWITCHING

In this work, force terms $f(x, \theta)$ are derived from a sawtooth potential $V(x)$ as shown in Figure 2 (we assume $L = 1$ without any loss of generality). More specifically, $f(x, 1) = -V'(x) + b$ and $f(x, 0) = -V'(x) - a$, where $V(x)$ is given by

$$V(x) = \begin{cases} \frac{1}{1+2\alpha}(2x + 1) \text{for } x \bmod 1 \in [-\frac{1}{2}, \alpha] \\ -\frac{1}{1+2\alpha}(2x - 1) \text{for } x \bmod 1 \in [\alpha, \frac{1}{2}] \end{cases}, \tag{5}$$

and $\alpha \in (-\frac{1}{2}, \frac{1}{2}) \backslash \{0\}$ to ensure *asymmetry*. The periodicity condition is satisfied as $V(x + 1) = V(x)$, which makes the force $f(x)$ periodic as well. This choice of potential is motivated by the simplicity in its practical implementation (need to just change the force bias to enable flashing) as well as that it allows for a closed-form steady-state solution of the associated DCK (4). We incorporate state feedback by treating the switching rates as control parameters and designing the feedback laws $\lambda(x, 0) =: \mu(x)$ and $\lambda(x, 1) =: \nu(x)$ to be explicit functions of the realized (or measured) state x. In this work, for simplicity in analysis we assume that $\mu(x)$ and $\nu(x)$ are periodic with the same spatial period 1 as the potential $V(x)$. For a given initial condition (y, θ_0) at time t_0, if we represent $p(x, 1, t | y, \theta_0, t_0)$ and $p(x, 0, t | y, \theta_0, t_0)$ by $P^+(x, t)$ and $P^-(x, t)$ respectively, then the DCK (4) becomes

$$\dot{P}^+ = -[(f(x) + b)P^+]' + DP^{+''} + \mu(x)P^- - \nu(x)P^+$$
$$\dot{P}^- = -[(f(x) - a)P^-]' + DP^{-''}$$
$$-\mu(x)P^- + \nu(x)P^+. \tag{6}$$

If we represent the total probability $P^+(x, t) + P^-(x, t)$ by $\hat{P}(x, t)$ and the average bias $bP^+(x, t) - aP^-(x, t)$ by $\hat{\Pi}(x, t)$, then (6) in these variables becomes

$$\dot{\hat{P}} = -[f(x)\hat{P} + \hat{\Pi} - D\hat{P}']' := \hat{J}'(x, t)$$
$$\dot{\hat{\Pi}} = -[ba\hat{P} + (f(x) + \beta)\hat{\Pi}]' + D\hat{\Pi}''$$
$$+ \eta(x)\hat{P} - \tau^{-1}(x)\hat{\Pi}, \tag{7}$$

where $\beta = b - a$, $\eta(x) = a\nu(x) - b\mu(x)$, and $\tau^{-1}(x) = \mu(x) + \nu(x)$. After noting that the above pde has spatially periodic coefficients, it is easy to verify that if $(\hat{P}(x, t), \hat{\Pi}(x, t))$ is a solution, then so is $(P(x, t), \Pi(x, t))$ where $P(x, t) = \sum_{n=-\infty}^{\infty} \hat{P}(x+n, t)$ and $\Pi(x, t) = \sum_{n=-\infty}^{\infty} bP^+(x + n, t) - aP^-(x + n, t)$. Thus $(P(x, t), \Pi(x, t))$ satisfies the pde (7). Also, note that the above definition implies periodicity in $P(x, t) = P(x + 1, t)$ and also that $\int_0^1 P(x, t) dx = 1$ for all t (Note similarly $J(x, t) = \sum_{n=-\infty}^{\infty} \hat{J}(x+n, t)$ is also periodic). This change of variables is useful since it has periodic boundary conditions, for which it is easy to obtain the steady-state (stationary) solution (On the other hand, for $\hat{P}(x, t)$ we do not expect a stationary solution, since we expect the mean of the

particle position to drift incessantly to the right with time). The stationary state $P(x) = \lim_{t\to\infty} P(x,t)$ and $\Pi(x) = \lim_{t\to\infty} \Pi(x,t)$ are given by substituting $\dot{P} = 0$ and $\dot{\Pi} = 0$) in (7), that is,

$$[f(x)P(x) + \Pi - DP'(x)]' := J'(x) = 0,$$
$$-[baP(x) + (f(x) + \beta)\Pi(x)]' + D\Pi''(x)$$
$$+\eta(x)P(x) - \tau^{-1}\Pi(x) = 0, \qquad (8)$$

and since $J'(x) = 0$, therefore the probability current $J(x) \equiv J^{st}$ is a constant. Hence we have,

$$\Pi(x) = J^{st} + D\partial_x P(x) - f(x)P(x). \qquad (9)$$

We use (9) to eliminate $\Pi(x)$ from (8), and obtain the following ordinary differential equation:

$$D^2 P'''(x) - D[\beta P''(x) + [f(x)P(x)]'' + [f(x)P'(x)]']$$
$$+\beta[f(x)P(x)]' + [f^2(x)P(x)]' - \tau^{-1}(D+ba)P'(x)$$
$$+(\eta + \tau^{-1}f(x))P(x) = (f'(x) + \tau^{-1})J^{st}. \quad (10)$$

Since $P(x)$ is periodic, it suffices to solve (10) in $[x_0, x_0 + 1]$ $\forall x_0 \in [-\frac{1}{2}, \alpha]$. Note that force $f(x)$ is piecewise constant of the form $f(x) = \sum_{j=1}^{3} f_j \Theta_j$, where $f_1 = f_3$, $\Theta_1 = \Theta(\alpha - x)$, $\Theta_2 = \Theta(x - \alpha) - \Theta(x - \frac{1}{2})$, $\Theta_3 = \Theta(x - \frac{1}{2})$, and $\Theta(x)$ is the spatial-domain step function. If we choose the feedback laws to have the same structure, that is, $\mu(x) = \sum_{j=1}^{3} \mu_j \Theta_j$ and $\nu(x) = \sum_{j=1}^{3} \nu_j \Theta_j$ with $\mu_1 = \mu_3$ and $\nu_1 = \nu_3$, then it can be expected that the solution will be of the form given by $P(x) = \sum_{j=1}^{3} p_j(x)\Theta_j$ where $p_1(x) = p_3(x)$. On substituting these structures of $f(x), \mu(x), \nu(x)$, and $p(x)$ in (10), we obtain the following two third-order linear odes

$$D^2 p_i'''(x) - D(\beta + 2f_i)p_i''(x)$$
$$+(\beta f_i + f_i^2 - (ab + D\tau_i^{-1}))p_i'(x)$$
$$+(\eta_i + f_i\tau_i^{-1})p_i(x) - J^{st}\tau_i^{-1} = 0 \qquad (11)$$

where $i \in \{1, 2\}$ and $\tau_i^{-1} = \mu_i + \nu_i$, and the following six conditions (see appendix for details)

$$p_2(\alpha) = p_1(\alpha), p_1(-\frac{1}{2}) = p_2(\frac{1}{2}),$$
$$D(p_2'(\alpha) - p_1'(\alpha)) = f_2 p_2(\alpha) - f_1 p_1(\alpha)$$
$$D(p_2'(\frac{1}{2}) - p_1'(-\frac{1}{2})) = f_2 p_2(\frac{1}{2}) - f_1 p_1(-\frac{1}{2})$$
$$D^2(p_2''(\alpha) - p_1''(\alpha)) = 2D(f_2 p_2'(\alpha) - f_1 p_1'(\alpha))$$
$$-(f_2^2 p_2(\alpha) - f_1^2 p_1(\alpha)) + J^{st}(f_2 - f_1),$$
$$D^2(p_2''(\frac{1}{2}) - p_1''(-\frac{1}{2})) = 2D(f_2 p_2'(\frac{1}{2}) - f_1 p_1'(-\frac{1}{2}))$$
$$-(f_2^2 p_2(\frac{1}{2}) - f_1^2 p_1(-\frac{1}{2})) + J^{st}(f_2 - f_1). \quad (12)$$

Note that we require six conditions for the sixth order ode in (11); however one more condition is needed to evaluate the constant J^{st}. This is obtained by requiring $\int_0^1 p(x)dx = 1$ which results in the following condition

$$1 = \left[\frac{(\alpha + \frac{1}{2})\tau_1^{-1}}{\eta_1 + f_1\tau_1^{-1}} + \frac{(\frac{1}{2} - \alpha)\tau_2^{-1}}{\eta_2 + f_2\tau_2^{-1}}\right] J^{st}$$
$$-D^2 \left[\frac{(p_1''(\alpha) - p_1''(-\frac{1}{2}))}{\eta_1 + f_1\tau_1^{-1}} + \frac{p_2''(\frac{1}{2}) - p_2''(\alpha)}{\eta_2 + f_2\tau_2^{-1}}\right]$$
$$+D\left[\frac{2f_1 + \beta}{\eta_1 + f_1\tau_1^{-1}}(p_1'(\alpha) - p_1'(-\frac{1}{2}))\right.$$
$$+\left.\frac{2f_2 + \beta}{\eta_2 + f_2\tau_2^{-1}}(p_2'(\frac{1}{2}) - p_2'(\alpha))\right]$$
$$-\frac{f_1^2 + \beta f_1 - (ab + D\tau_1^{-1})}{\eta_1 + f_1\tau_1^{-1}}((p_1(\alpha) - p_1(-\frac{1}{2}))$$
$$-\frac{f_2^2 + \beta f_2 - (ab + D\tau_2^{-1})}{\eta_2 + f_2\tau_2^{-1}}((p_1(\alpha) - p_1(-\frac{1}{2}))(13)$$

The solution of the linear odes (11) are of the form

$$p_i(x) = \Gamma_{i1}e^{\lambda_{i1}x} + \Gamma_{i2}e^{\lambda_{i2}x} + \Gamma_{i3}e^{\lambda_{i3}x} + \frac{J^{st}\tau_i^{-1}}{\eta_i + f_i\tau_i^{-1}}, \quad (14)$$

where the modes $\lambda_{ij}, j \in \{1, 2, 3\}$ are the three roots of the characteristic equations

$$D^2\lambda_i^3 - D(\beta + 2f_i)\lambda_i^2 + (\beta f_i + f_i^2 - (ab + D\tau_i^{-1}))\lambda_i$$
$$+(\eta_i + f_i\tau_i^{-1}) = 0, \quad (15)$$

and the constants Γ_{ij} ($i \in \{1, 2\}$ and $j \in \{1, 2, 3\}$) and J^{st} can be determined by substituting the conditions (12) and (13) in (14). Note that the design parameters are the feedback laws $\mu(x)$ and $\nu(x)$; and therefore by designing parameters μ_i and ν_i ($i \in \{1, 2\}$), one can change the solution of (11) and thereby effecting a change in the transport characteristics of the flashing ratchet. A notable difference in our work is that we derive the steady-state probability distribution of the particle position by using the DCK equations while earlier works [3], [4] assume such a distribution.

IV. SIMULATION RESULTS

In this section, we demonstrate the advantage of the feedback control by designing the control parameters such that the average steady-state velocity of the particle is increased. The average velocity at time t is defined as $< v(t) > = \frac{d}{dt}\int_{-\infty}^{\infty} x\hat{P}(x,t)dx$; which is given by

$$< v(t) > = \sum_{n=-\infty}^{\infty} \int_0^1 \hat{J}(x,t)dx = \int_0^1 J(x,t)dx (16)$$

Thus as $t \to \infty$ (steady-state), $< v_\infty > = J^{st}$, the steady-state value for $J(x,t)$. This implies that design parameters μ_i and ν_i that result in higher values of J^{st}
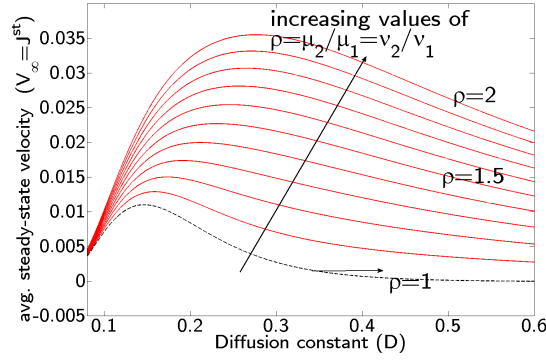
Fig. 3. Improvement in average steady-state velocity of the particle under flashing Brownian ratchet by applying state-feedback control. For both feedback (solid, $\rho > 1$) and no-feedback (dashed, $\rho = 1$) cases, the following parameters were assumed: asymmetry $\alpha = 0.25$, up-bias $b = 0.693$, down-bias $a = 1.443$, up-switching rate $\mu_1 = 0.7506$, and down-switching rate $\nu_1 = 0.3605$. For the feedback case $(\mu_2, \nu_2) = \rho(\mu_1, \nu_1)$, while for the no-feedback case $(\mu_2, \nu_2) = (\mu_1, \nu_1)$.

determined by (11)-(14) lead to higher average steady-state velocities of the particle. Figure 3 shows that with feedback, the average steady-state velocities are significantly higher than those obtained without feedback. In this simulation, all parameters for feedback and no-feedback case were kept identical except for the design variables. For state-feedback case, the switching rates depended on the state locations ($\mu_2 = \rho\mu_1$, $\nu_2 = \rho\nu_1$) (where ρ was incremented from 1.1-2 at steps of 0.1); while for the no-feedback case the switching rates were independent of the state-locations ($\mu_2 = \mu_1$, $\nu_2 = \nu_1$). The parameters μ_1 for the two cases were chosen the same (and likewise for the ν_1 parameters). This feedback scheme increases the switching rate, whenever it finds the state-location at the steep part of the potential (i.e. during opposing force); and thus achieves higher average velocities.

V. DISCUSSION AND CONCLUSIONS

As discussed earlier, the study in this article yields an interesting hypothesis on how motor proteins can enhance the speed of transport of cargo by using an intrinsic feedback scheme that alters the rate of switching between two ratchet potentials. Note that if we set $\eta(x) = 0$ in (8), the rates $\mu(x)$ and $\nu(x)$ do not appear separately but only their sum $\tau^{-1}(x) = \mu(x) + \nu(x)$ determines the equation. The function $\eta(x) = b\mu(x) - a\nu(x)$ is indicative of the average bias value over the underlying sawtooth potential $V(x)$. Therefore, typically for constant switching rates strategies, η is typically chosen to be zero since this bias

value can be absorbed into the potential $V(x)$. In such a case, since the model does not distinguish between the up and down rates (μ and ν), this provides a good implementation insight - that choose μ and ν such that $\frac{\mu}{\nu} = \frac{a}{b}$. The above arguments hold even when the switching rates are state dependent; however the effects are not as clear as the potential $V(x)$ gets augmented by another function $\eta(x)$ and not a constant. In the simulations presented above we chose parameters such that $\eta(x) = 0$, and therefore the results herein demonstrates the increase in velocity due to feedback even when there is no modification of the underlying potential. This is in agreement with the fact that a motor protein can achieve higher speeds of transport simply by restricting or enabling attachment/detachment of ATP/ADP like molecules depending on conformational changes (and hence affecting the switching rates) in the motor-protein, while leaving the underlying potential unaltered. Experiments to support this hypothesis is a part of the future work.

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