Fluctuating noise drives Brownian transport

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The transport properties of Brownian ratchet were studied in the presence of stochastic intensity noise in both overdamped and underdamped regimes. In the overdamped case, an analytical solution using the matrix-continued fraction method revealed the existence of a maximum current when the noise intensity fluctuates on intermediate timescale regions. Similar effects were observed for the underdamped case by Monte Carlo simulations. The optimal time-correlation for Brownian transport coincided with the experimentally observed time-correlation of the extrinsic noise in Escherichia coli gene expression and implied the importance of environmental noise for molecular mechanisms.

Keywords: stochastic process; Brownian transport; stochastic gene expression; superstatistics

1. INTRODUCTION

Noise-induced phenomena are attracting much attention not only in engineering but also in molecular biology. Counter-intuitively, noise can enhance system performance by increasing transmission and synchronization of information through stochastic resonance [1–6] and noise-induced synchronization [7–10].

For example, molecular systems function efficiently in nano-scale environments under multi-scale noise through thermal and other environmental fluctuations [11–14]. This efficiency should not be interpreted by assuming steady-state or Gaussian distribution. A recent single-cell observation of Escherichia coli revealed that the protein copy number does not obey the gamma distribution [15], and its stationary distribution can be approximated by superstatistics (i.e. the superposition of multiple statistical models; see equation (1.1) and §4). Chabot et al. revealed that the cellular variability in gene expressions comes from temporal (periodic) noise which is related to circadian oscillation [16]. In accordance with such experimental observations, theoretical studies also conclude that biochemical noise is not Gaussian to facilitate enhanced functionality [17,18]. Both experimental and theoretical approaches suggest fundamental roles of noise-enhanced phenomena to render efficient molecular systems.

In this paper, we investigate the efficiency of Brownian motor [19,20] (or a ratchet transport) under a noisy, non-equilibrium state. It is known that the violation of detailed balance induces a transport effect, which is a model for many biological mechanisms including ion pumps [21–23] that use adenosine triphosphate (ATP) for transport. (In theory, however, the conformational fluctuation of such pumps can facilitate transport even without ATP [24].)

Brownian transport has been studied intensively including in mass separation [25], electron transport in a quantum ratchet [26], transport of atoms in optical traps [27], a random walker model [28] and non-Gaussian noise models [29,30] (for more details, see comprehensive reviews [20,31]). One of the most popular ratchet models is the correlation ratchet in which Brownian particles in a ratchet potential are driven by the addition of white and coloured noise. The model studied here is a ratchet driven by the multiplication of white and coloured noise. Let us introduce our model more formally.

Superstatistics with temporal and/or spatial fluctuations [32–35] is used to explain non-Gaussian distributions [36,37] in applied physics. This concept is also seen in stochastic processes in which noise fluctuation is treated in a static way [33,38–43]. The superstatistical stochastic process calculates a stationary distribution \( P_{st}(x) \) by assuming that the noise fluctuates over a long timescale (i.e. very slowly):

\[
P_{st}(x) = \int_0^\infty dDP_{st}(x|D)P(D),
\]

where \( P_{st}(x|D) \) is the stationary distribution given the noise intensity \( D \) and \( P(D) \) is the distribution of \( D \). Equation (1.1) fits in the Bayesian framework by considering \( P_{st}(x) \) and \( P(D) \) as posterior and prior distributions, respectively.

We model temporal noise-intensity fluctuation dynamically and modulated the intensity of white Gaussian noise by the Ornstein–Uhlenbeck process in overdamped Langevin equations [44,45]:

\[
\dot{x} = -V'(x) + s\xi_s(t)
\]

and

\[
\dot{s} = -\gamma(s - \alpha) + \sqrt{\gamma}\xi_s(t).
\]
Here, $V(x)$ is the potential, $\alpha$ is the mean of the Ornstein–Uhlenbeck process, $\gamma$ is the relaxation rate $(\gamma > 0)$, and $\xi_j(t)$ and $\xi_i(t)$ are white Gaussian noise with the correlation:

$$\langle \xi_j(t) \xi_j(t') \rangle = 2D_s \delta(t - t')$$

and

$$\langle \xi_i(t) \xi_i(t') \rangle = 2D_s \delta(t - t').$$

We call the term $s(t)\xi_j(t)$, the stochastic intensity noise (SIN) because the noise intensity is governed by a stochastic process. SIN is the multiplicative term of white and coloured noise, and is qualitatively different from white noise systems driven by SIN are in non-equilibrium.

In the context of Brownian transport, Reimann et al. [46] first studied the transport effect with sinusoidal noise-intensity modulation. Our work differs from this and succeeding studies that employed a discrete dichotomous noise or a deterministic periodic signal [46–48]; in our model, fluctuations are governed by a continuous stochastic process (the Ornstein–Uhlenbeck process). There exist similar models. Borromeo et al. [49] studied a current generated by two symmetric coloured noises, the Ornstein–Uhlenbeck noise and its time-delayed version, and observed Maxwell’s demon-like phenomenon. Morgado et al. [50] investigated temporal heterogeneity in the Poisson mechanism. Our model focuses on a multiplicative rather than an additive effect, because biological phenomena are governed by multiplication (see §4). This distinction highlights the importance of SIN-induced transport.

In our calculations, we investigated the effect of four controllable parameters on the current:

- $\gamma$ (the relaxation rate in equation (2.2));
- $Q$ (the effective noise intensity in equation (2.6));
- $\rho$ (the squared variation coefficient in equation (2.7));
- $\mu$ (the scaled mass in equation (2.1)).

Although $D_s$ (the noise-intensity in equation (2.1)) is also a controllable parameter, we kept it constant ($D_s = 1$) throughout the paper. The squared variation coefficient $\rho$, which is generally defined as the ratio of the squared mean to the variance, characterizes the deviation of the Gaussian noise distribution by the kurtosis. The overdamped case is calculated using the matrix-continued fraction method (MCFM) and Monte Carlo (MC) simulations. The calculations reveal that the current is maximum at adequate $\gamma$ and $Q$. This result concurs with resonant activation [51] and noise-enhanced stability [52,53] in the escape problem. Our main result is the enhanced transport capability in intermediate time-correlation regions. This has an important biological implication. The time-correlation of extrinsic noise (i.e. environmental fluctuation) with gene expression in E. coli is on the order of cell cycle length [54]. By fitting the timescale of our model to the E. coli model in [55], we found that the time-correlation of extrinsic noise coincides with the region of enhanced transport. It is a theoretical backup of the tacit exploitation of environmental fluctuation by biological organisms.

**Figure 1.** A ratchet potential of equation (2.3). The dashed and solid arrows indicate the directions of the current in the correlation ratchet (driven by additive white and coloured noise) and the ratchet (driven by SIN), respectively. (Online version in colour.)

### 2. METHODS

#### 2.1. Brownian particles

Brownian particles are subject to noise-intensity fluctuations represented by

$$\mu \dot{x} = -\dot{x} - V'(x) + s\xi_j(t)$$

and

$$\dot{s} = -\gamma(s - \alpha) + \sqrt{2\gamma}\xi_i(t),$$

where the scaled mass $\mu$ is introduced into equation (1.2) for a study of a mass separation effect, and meanings of $V(x)$ are the same as in equation (1.2). We used the same ratchet potential function as used in previous studies [56,57]

$$V(x) = \frac{1}{2\pi} \left\{ \sin(2\pi x) + \frac{1}{4} \sin(4\pi x) \right\} + Fx,$$

with a periodicity $V(x + 1) = V(x)$ ($F = 0$), where $F$ is the load. Figure 1 shows the potential with no load ($F = 0$), where the dashed and solid arrows indicate the normal current direction for the correlation ratchet [56,57] and for the ratchet driven by SIN, respectively.

The current direction for the SIN case is identical to that in [47] in which the noise intensity is modulated by a random dichotomous process. In equation (2.2), the relaxation rate $\gamma$ denotes the inverse of a timescale (time-correlation). When the noise intensity fluctuates with a longer timescale ($\gamma = 0$), systems driven by SIN locally equilibrate and hence a current is not generated in accordance with the second law of thermodynamics. Likewise, SIN reduces to white noise (with a noise intensity $Q$) when the noise-intensity fluctuates very rapidly ($\gamma \to \infty$) [44], which also indicates that the current vanishes.

For equation (2.2), the stationary distribution $P_{st}(s)$ of the intensity-modulation term $s$ is given by

$$P_{st}(s) = \frac{1}{\sqrt{2\pi D_s}} \exp \left\{ -\frac{1}{2D_s} (s - \alpha)^2 \right\},$$

A calculation of the correlation function of SIN yields [45]

$$\langle s(t)\xi_j(t)s(t')\xi_i(t') \rangle = 2QS\delta(t - t').$$
show trajectories of SIN with where $k$ increases with increasing
$D_s$ while keeping the effective intensity $Q = D_s(D_i + \alpha^2)$ constant. (Online version in colour.)

with
\[
Q = D_s(D_i + \alpha^2),
\]  
(2.6)
where $Q$ expresses the effective noise intensity and $D_s$ and $D_i$ are the noise intensities of $\xi_x(t)$ and $\xi_s(t)$, respectively (equations (1.4) and (1.5)). Here, we introduce the squared variation coefficient $\rho$ of the noise-intensity fluctuations [45]:
\[
\rho = \frac{D_s}{\alpha^2},
\]  
(2.7)
which denotes the squared ratio of the standard deviation to the mean of equation (2.4). Figure 2a–d show trajectories of SIN with $\rho = 0.01$, 0.1, 1, and 100, respectively. All share the same effective noise intensity $Q$ (the same variance). For $\rho = 0$, SIN reduces to white Gaussian noise with a noise intensity $Q = D_i\alpha^2$. On increasing $\rho$ (figure 2e–h), the noise-intensity fluctuations become larger and the distribution of SIN deviates from the Gaussian distribution. To quantify the deviation, we calculate the kurtosis of SIN, which is a measure of heavy tails in probability density functions. The kurtosis $\kappa$ of SIN (i.e. $s(t)\xi_x(t)$) is given by (appendix A)
\[
\kappa = \frac{\left\langle (s(t)\xi_x(t))^4 \right\rangle}{\left\langle (s(t)\xi_x(t))^2 \right\rangle^2},
\]  
(2.8)
\[
= 9 - \frac{6}{\left(1 + \rho \right)^2} \quad (0 \leq \rho < \infty),
\]
where $\kappa$ depends only on the squared variation coefficient $\rho$ having a crucial effect on the statistical properties of SIN. Equation (2.8) shows that the kurtosis is 3 for $\rho = 0$ and $\kappa$ increases with increasing $\rho$, giving a flatter distribution. Figure (2.8) is plotted by the solid curve in figure 3 in which the filled circles denote the kurtosis calculated by MC simulations.

3. RESULTS
In equations (2.1) and (2.2), our model has four parameters ($\gamma$, $\alpha$, $D_i$ and $D_s$) in terms of noise properties.

\[
\alpha = \sqrt{\frac{Q}{D_s(1 + \rho)}}, \quad D_i = \frac{\rho Q}{D_s(1 + \rho)}.
\]  
(3.1)

Performing model calculations based on the MCFM and MC simulations, we studied the dependence of the current on $\gamma$, $\alpha$, $Q$ in the overdamped case ($D_s$ is set to $D_s = 1$ throughout the paper). In the underdamped case, we additionally investigated the dependence of the
current on the scaled mass $\mu$ (equation (2.1)) with MC simulations. MC simulations were performed with the Euler-forward method with a time resolution of $\Delta t = 10^{-4}$ (for details of the method, see [58]).

### 3.1. Overdamped case

We first calculated the current $J$ for the overdamped case ($\mu = 0$ in equation (2.1)). For $t \to \infty$, the stationary distribution $P_{st}(x,s)$ of $(x,s)$ has to satisfy the stationary Fokker–Planck equation (FPE)

$$\mathbf{L}_{FP}P_{st}(x,s) = 0, \quad \text{(3.2)}$$

where $\mathbf{L}_{FP}$ is an FPE operator:

$$\mathbf{L}_{FP} = \frac{\partial}{\partial x} V'(x) + D_x \frac{\partial^2}{\partial x^2} s^2 + \gamma \left( \frac{\partial}{\partial s} (s-\alpha) + D_s \frac{\partial^2}{\partial s^2} \right). \quad \text{(3.3)}$$

Since equation (3.2) is not written in terms of potential forms, we cannot calculate the stationary distribution in a closed form. Consequently, we used the MCFM to solve equation (3.2), which expands $P_{st}(x,s)$ in terms of a complete orthonormal set. The MCFM is a common technique for stochastic processes and is widely used to solve FPEs (see [58] and references therein). Considering the periodicity of the potential ($V'(x+1) = V'(x)$) and domain ($x \in (-\infty, \infty)$ and $s \in (-\infty, \infty)$), we expanded the stationary distribution $P_{st}(x,s)$ in a Fourier series for $x$ and the Hermite function for $s$:

$$P_{st}(x,s) = \psi_0(s) \sum_{k=-M_k}^{M_k} \sum_{n=0}^{M_n} C_{k,n} \exp(2\pi ikx) \psi_n(s) \quad \text{(3.4)}$$

Here, $C_{k,n}$ are expansion coefficients, $M_k$ and $M_n$ are truncation numbers on which the precision of obtained solutions depends, and $\psi_n(s)$ is the Hermite function satisfying the orthonormality relation

$$\langle \psi_n(s) \psi_m(s) \rangle = \delta_{n,m}.$$

$$\psi_n(s) = \left( \frac{1}{2\pi D_x} \right)^{1/4} \sqrt{\frac{1}{2^n n!}} H_n(s) \eta \exp \left( -\frac{1}{2} \eta^2 \right), \quad \eta = \frac{1}{\sqrt{2D_s}} (s-\alpha), \quad \text{(3.5)}$$

where $H_n(s)$ is the $n$th Hermite polynomial. Multiplying equation (3.2) by $\exp(-2\pi ikx)\psi_n(s)/\psi_n(s)$ and integrating over $x$ and $s$, we obtain a linear algebraic equation in terms of $C_{k,n}$, which can be solved by the MCFM (appendix B). The current $J$ is calculated using

$$J(x) = \frac{1}{\sqrt{2\pi}} \int_0^\infty ds J_x(x,s) \quad \text{(3.6)}$$

where $J_x(x,s)$ is the probability current in the $x$-direction due to the continuity equation $\partial_t P + \partial_x J_x + \partial_s J_s = 0$:

$$J_x(x,s) = \left( -V'(x) - D_x s^2 \frac{\partial}{\partial x} \right) P_{st}(x,s). \quad \text{(3.7)}$$

By substituting equation (3.4) into equation (3.6), the current $J$ can be expressed in terms of $C_{k,n}$:

$$J = \frac{1}{2} (C_{-1,0} + C_{1,0}) - \frac{1}{4} (C_{-2,0} + C_{2,0}) - FC_{0,0}. \quad \text{(3.8)}$$

The current given by equation (3.8) does not vanish even when there is no load (i.e. $F=0$) due to the broken detailed balance.

In practical calculations of equation (3.8), we increased the truncation numbers $M_k$ and $M_n$ in equation (3.4) until the current $J$ converged. We also performed MC simulations to verify the reliability of the MCFM, where the velocity is given by $v = [x(T) - x(0)]/T$ ($T = 10^2$). The calculation was repeated 100 times and the average velocity was determined. Below, we calculate the dependence of the current $J$ on the relaxation rate $\gamma$ (figure 4), the effective noise intensity $Q$ (figure 5) and the squared variation coefficient $\rho$ (figure 6).
We first show the current $J$ as a function of the relaxation rate $g$ (equation (1.3)). In figure 4, $g$ is plotted against the current $J$ for two sets of parameters: case (a) $D_x = 1$ and $Q = 0.2$ (figure 4a), and case (b) $D_x = 1$ and $Q = 1$ (figure 4b). The relationship was computed for four values of $r$ (the squared variation coefficient): $r = 0.1$, $1$, $10$ and $1$ (the case $r = 1$ corresponds to $a = 0$ and $D_x = Q/D_x$). In case (a), $J$ became a maximum at an intermediate $g$, while the current vanished for both $g \to 0$ and $g \to 1$. The small current at $r = 0.1$ was expected because a small $r$ corresponds to weak noise fluctuations. Because larger $r$ means larger fluctuations (the kurtosis monotonically increases as a function of $r$, as shown in figure 3), it is natural that the current increases as $r$ increases. However, $J$ in the range $g > 10$ shows a different tendency and it is higher when $r = 1$ than when $r = 10$ or $r = \infty$. This is due to the noise-intensity modelling in equation (2.2): specifically, $s(t)$ in equation (2.2) for small $r$ rarely has negative values, whereas $s(t)$ for large $r$ has negative as well as positive values. For large $\gamma$ cases, the ‘effective’ relaxation rate might be measured by $\langle |s(t)||s(t')| \rangle$ rather than by $\langle s(t)s(t') \rangle$, which indicates that the effective relaxation rates for larger $\rho$ cases are larger than their actual values. In figure 4, the results obtained by the MCFM (lines) are always in agreement with MC simulations (symbols), which indicates the reliability of the MCFM. The MC simulations tended to converge for smaller $Q$ cases because $v$ is more centred on the mean (thin distributions) when the effective noise intensity is smaller. We also note the difference between our model and that of [46] where noise-intensity is modulated by a deterministic sinusoidal signal. We found that the width of peaks tends to be wider in our model, which is a consequence of the fact that the power spectrum of Ornstein–Uhlenbeck noise has the Lorentzian function whereas that of a sinusoidal function is a delta-peaked function.

We next show the current $J$ as a function of the effective noise intensity $Q$ (equation (2.6)). Since the effect of the relaxation rate $\gamma$ varies depending on the squared variation coefficient $\rho$ (as shown above), we removed
the $\gamma$ dependence of the current $J$ by taking the maximum in terms of $\gamma$:

$$J_{\text{max}} = J_{\text{max}}(D_x, Q, \rho) = \max_{\gamma} J(D_x, \gamma, Q, \rho)$$  \hspace{1cm} (3.9)

and

$$\gamma_{\text{max}} = \gamma_{\text{max}}(D_x, Q, \rho) = \arg\max_{\gamma} J(D_x, \gamma, Q, \rho).$$  \hspace{1cm} (3.10)

Here, $J_{\text{max}}$ and $\gamma_{\text{max}}$, respectively, denote the maximum current and $\gamma$ when the current is a maximum. Figure 5a,b shows plots of $J$ against $J_{\text{max}}$ and $\gamma_{\text{max}}$ for $D_x = 1$, respectively. Again, computations were performed for four values of $\rho$. In figure 5a, $J_{\text{max}}$ has maxima as a function of $Q$; the magnitude of this maxima is small for $\rho = 0.1$, as in figure 4. Transport effects are robust in terms of the noise intensity $Q$, because the current for $Q = 2$ still exhibits half the maximum current (around $Q = 0.2$) for large $\rho$ cases. Figure 5b shows $\gamma_{\text{max}}$ (i.e. the relaxation rate yielding the maximum current) as a function of $Q$. For all four values of $\rho$, $\gamma_{\text{max}}$ has a maximum value around $Q = 0.1$ and decreases with increasing $Q$. This result shows that the noise intensity has to fluctuate over a long timescale to enhance the transport capability in noisy environments.

We also investigated the dependence of $\rho$ on $J_{\text{max}}$ while keeping the other parameters constant. Figure 6a shows $J_{\text{max}}$ (equation (3.9)) as a function of $\rho$ with $D_x = 1$ and five values of $Q$ (the effective noise intensity): $Q = 0.1, 0.2, 0.4, 0.8$ and $1.6$. $J_{\text{max}}$ increases monotonically; the increase exhibits sigmoid-like behaviour in terms of $\log \rho$, indicating that $J_{\text{max}}$ is an extremely nonlinear function in terms of $\rho$. Figure 6b shows the dependence of $J_{\text{max}}$ on the kurtosis $\kappa$ (equation (2.8)). Although $J_{\text{max}}$ still exhibits nonlinearity as a function of $\kappa$, its nonlinearity is much smaller than that of $\rho$. This result shows that the kurtosis can be used as an index parameter for Brownian transport driven by noise-intensity fluctuations.

3.2. Underdamped case

We next investigated Brownian transport (equations (2.1) and (2.2)) in the underdamped regime, especially from the viewpoint of a mass separation effect [25]. Although we could use the MCFM for the overdamped case, the MCFM for an underdamped FPE did not yield stable solutions in terms of the current (data not shown) so that we used MC simulations only. The underdamped model includes an extra parameter $\mu$ (scaled mass) in addition to the four parameters ($\gamma$, $\rho$, $Q$ and $D_x$). The velocity is given by $v = |x(T) - x(0)| / T$ ($T = 10^3$). The calculation was repeated 100 times to obtain the current as the average velocity.

We first show the current $J$ as a function of the scaled mass $\mu$. Figure 7 shows the dependence of the current $J$ on $\mu$ for two values of $\gamma$ (case (a) $\gamma = 1$ (figure 7a) and case (b) $\gamma = 30$ (figure 7b)), where the other parameters are $D_x = 1$, $Q = 0.2$, $F = 0$ and $\rho = 1$ (circles) or $\rho = \infty$ (squares). In case (a), the current decreases monotonically and the current for $\rho = \infty$ always exceeds that for $\rho = 1$. In contrast, in case (b), the current of $\rho = \infty$ is always smaller than that of $\rho = 1$ and the relation between the magnitudes for $\rho = 1$ and $\infty$ differs from that of case (a). As shown in figure 5, the 'effective' relaxation rate for larger $\rho$ is larger than the actual relaxation rate. This is the reason why converse magnitude relaxation occurs between $\rho = 1$ and $\infty$ in case (b).

We next show the dependence of the average current $J$ on $\gamma$ for two values of $Q$ (the effective noise intensity): case (a) $Q = 0.1$ ($D_x = 1$, $\rho = \infty$ and $F = 0.025$) (figure 8a) and case (b) $Q = 1$ ($D_x = 1$, $\rho = \infty$ and $F = 0.006$) (figure 8b). In both cases, the load F (case (a) $F = 0.025$ and case (b) $F = 0.006$) increased the ratchet potential for larger values of $x$ and the value of $F$ was determined such that particles of $\mu = 0.01$ and 1 move in opposite directions. Figure 8 shows $J$ of $\mu = 0.01$ (circles) and $\mu = 1$ (squares) for $Q = 0.1$ (figure 8a) and $Q = 1$ (figure 8b), where the lines show the MCFM results for the overdamped case ($\mu = 0$). We include the $\mu = 0.01$ case along with the MCFM result to show that results of the underdamped

Figure 7. Current $J$ as a function of $\mu$ using MC simulations for (a) $\gamma = 1$ and (b) $\gamma = 30$. The other parameters are $D_x = 1$, $Q = 0.2$ and $F = 0$ with $\rho = 1$ (circles) and $\rho = \infty$ (squares). Lines are included as a guide to the eye only. (Online version in colour.)
case decrease asymptotically to the overdamped case as $\mu \to 0$. In cases (a) and (b), the current $J$ for $\mu = 0.01$ has positive values, unlike $J$ for $\mu = 1$, which is negative over the whole range of $\gamma$. $J$ for $\mu = 0.01$ has peaks at intermediate $\gamma$ values; however, the $\gamma_{\text{max}}$ values at which the current is a maximum are different in cases (a) and (b): $\gamma_{\text{max}}$ in case (a) ($Q = 0.1$) is around 10, whereas $\gamma_{\text{max}}$ in case (b) ($Q = 1$) is about 1. Since the currents for $\mu = 0.01$ and 1 move in the opposite directions, particles with $\mu = 0.01$ and 1 can be set apart due to the mass separation effect. To quantify the mass separation capability, we define $\Delta J$ as

$$\Delta J = J(\mu = 0.01) - J(\mu = 1), \quad (3.11)$$

where $\Delta J$ is a quantity of interest for the separation phenomenon. Systems with larger $\Delta J$ exhibit a better separation capability. Figure 8c shows $\Delta J$ for two cases (case (a) ($Q = 0.1$) and case (b) ($Q = 1$)) and the lines show locally weighted scatterplot smoothing (LOWESS) for each data. It clearly shows that $\gamma$ at which the mass separation capability is a maximum is different for the two $Q$ cases and that better mass separation is realized at smaller $\gamma$ values in the larger $Q$ case. This result shows that the mass separation capability is greater for slower environmental fluctuations when Brownian motors are subject to strong noise.

4. DISCUSSION

We investigated the statistical properties of SIN on Brownian ratchet and found that the current was enhanced for smaller $\gamma$ in both the overdamped and underdamped regimes (figures 5 and 8) when the effective noise-intensity $Q$ is larger. This result is intriguing because a smaller $\gamma$ corresponds to extrinsic fluctuations with a larger timescale. In single-cell experiments on *E. coli*, assuming that mRNA production is Poissonian and that the protein burst size has an exponential distribution, the protein copy number obeys the gamma distribution [15]:

$$P(x) = \frac{x^{a-1}e^{-x/b}}{\Gamma(a)b^a}, \quad (4.1)$$

where $a$ and $b$ are parameters. Observations [15] revealed that the fluctuations (extrinsic noise) in $a$ and $b$ are slow and the stationary distribution can be approximated as

$$P(x) = \int_0^\infty db \int_0^\infty da \frac{x^{a-1}e^{-x/b}}{T(a)b^a} P(a)P(b), \quad (4.2)$$

where $P(a)$ and $P(b)$ denote the distributions of $a$ and $b$, respectively. Note that equation (4.2) is equivalent to the description of superstatistics (see equation (1.1)). In stochastic gene expression, the intrinsic noise is rather well explained: its source is stochastic chemical reactions with a small number of molecules. In contrast, contribution of the extrinsic noise has not been well reasoned or modelled [59,60]. Stochastic gene expression is often modelled with Langevin equations, i.e. continuous approximation of the continuous-time Markov chain through Van Kampen’s expansion [61]. Many models assume that extrinsic noise affect the transcriptional, translational and degradation kinetics as in equation (4.2), which results in both drift terms and noise-intensity fluctuations of corresponding Langevin equations. The stochastic term of Langevin equations is often approximated with the additive white noise, and therefore, the extrinsic noise-induced fluctuation fits the overdamped case given by equation (2.1) and (2.2), assuming that the drift term fluctuation is negligible compared with that of the noise-intensity. Our calculations showed that environmental fluctuations should be slow to enhance the transport capability in noisy environments. That is, fluctuations in $a$ and $b$ in equation (4.1) occur over long timescales.

Lastly, let us show the correspondence of our calculations with actual timescales in biological experiments. Rosenfeld et al. [54] observed that the time correlation of extrinsic fluctuations in *E. coli* is in the order of cell cycle length $T_{cc}$. The deterministic part of the protein concentration $x$ generally obeys

$$\frac{dx}{dt} = f_* - \beta x, \quad (4.3)$$

where $f_*$ is a protein synthesis term (via translation) and $\beta$ is the degradation rate. In Langevin equations, the
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concluded that the time correlation of the extrinsic fluctuation is \( \tau = T_v \lambda / \log 2 \) (where \( T_v = 60 \text{min} \)). Because the ratchet potential given by equation (2.3) can be approximated by a quadratic function around the minima, equation (2.1) can be cast in the form of equation (4.3) with \( \beta \approx 10 \). Matching the timescales of these two systems by comparing the relaxation time (i.e., comparing \( \beta \) in the two cases), the time correlation of the extrinsic fluctuations observed in *E. coli* corresponds to \( \tau = 0.1 \) in our ratchet potential model. Figure 5 shows that \( T_{\text{max}} \) is in the approximate range 1–10, which implies that \( \tau_{\text{max}} = T_{\text{max}} = 0.1 \sim 1 \). Therefore, the extrinsic noise in the experimental observation is close to optimal for the transport effect.

Extrinsic noise has non-negligible time-correlation, leaving the system at non-equilibrium states. Although there remains a biochemical gap between gene expressions and ion transports, our result shows the biochemical advantage of exploiting extrinsic noise for gene regulation.

In summary, we investigated the transport properties of Brownian ratchet in both overdamped and underdamped regimes [44,45]. In the overdamped regime, our calculations by the MCFM and MC simulations revealed the existence of a maximum current as a function of \( \gamma \) (the relaxation rate) and \( Q \) (the effective noise intensity). The maximum current is induced at a lower relaxation rate \( \gamma \) for higher noise intensities. In the underdamped regime, MC calculations also showed a maximum for smaller \( \gamma \) when systems are subject to noisy environments. Consequently, the mass separation capability was also maximized for smaller \( \gamma \) in such cases. We continue the investigation of ratchet transport in specific biological models in ongoing studies.

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**APPENDIX A. KURTOSIS OF SIN**

We calculate kurtosis \( \kappa \) of SIN, as defined by

\[
\kappa = \frac{\langle s(t) \xi(t) \rangle^4}{\langle s(t) \rangle^2 \langle \xi(t) \rangle^2}.
\]

(A 1)

By using an independence relation between \( s \) and \( \xi \), and the Gaussian nature of \( \xi \), the numerator and denominator in equation (A 1) are given by

\[
\langle s(t) \xi(t) \rangle^4 = 3 \langle s(t) \rangle^4 \langle \xi(t) \rangle^2
\]

(A 2)

and

\[
\langle s(t) \rangle^2 = \langle u(t) \rangle^2 = D_s + \alpha^2.
\]

(A 3)

Let \( u(t) = s(t) - \alpha \). Since \( u(t) \) is a standard Ornstein–Uhlenbeck process with \( \langle u(t) \rangle = 0 \), the second- and fourth-order moments are \( \langle u(t) \rangle^2 = D_s \) and \( \langle u(t)^4 \rangle = 3 D_s^2 \), which yields

\[
\langle s(t) \rangle^4 = \alpha^4 + 6 \alpha^2 \langle u(t)^2 \rangle + \langle u(t)^4 \rangle
\]

\[
= \alpha^4 + 6 \alpha^2 D_s + 3 D_s^2,
\]

(A 5)

With equations (A 2)–(A 5), the kurtosis is calculated as

\[
\kappa = \frac{3(\alpha^4 + 6 \alpha^2 D_s + 3 D_s^2)}{(D_s + \alpha^2)^2}.
\]

(A 6)

Substituting \( \rho = D_s / \alpha^2 \) into equation (A 9), we obtain equation (2.8).

**APPENDIX B. MATRIX-CONTINUED FRACTION METHOD**

We explain the procedure of the MCFM in the overdamped case. Substituting equation (3.4) into equation (3.2), we obtain a linear algebraic equation:

\[
0 = C_{k,n} \left[ -n \gamma + 2 F \pi k_i - 4 \pi^2 D_s k^2 \left\{ \left( 2 + 2 D_s \left( n + \frac{1}{2} \right) \right) \right\} \right] + C_{k-1,n} \pi k_i + C_{k+1,n} \pi k_i + C_{k+2,n} \pi k_i - 4 C_{k,n+2} \pi^2 D_s k^2 \sqrt{(n + 2)(n + 1)}
\]

\[
- 4 C_{k,n-2} \pi^2 D_s k^2 \sqrt{n(n - 1)}
\]

\[
- 8 C_{k,n-1} \pi^2 D_s k^2 \sqrt{D_s n}
\]

\[
- 8 C_{k,n+1} \pi^2 D_s k^2 \sqrt{D_s (n + 1)}
\]

(B 1)

where the dimension of the linear algebraic equation (B 1) is \( (2 M_n + 1)(M_n + 1) \). We show the MCFM for equation (B 1), since a naive conversion of equation (B 1) yields an equation with second-nearest-neighbour coupling, which is not handled with the MCFM (the MCFM can treat only first-nearest-neighbour coupling). By introducing \( c_k = (C_{k,0}, C_{k,1}, \ldots, C_{k,M_n})^\top \), equation (B 1) is calculated as

\[
0 = \pi k i \mathbf{E} c_{k-2} + \pi k_i \mathbf{E} c_{k-1} + \left[ A - 4 \pi^2 D_s k^2 B \right] c_k + 2 F \pi k_i \mathbf{E} c_{k+1} + \frac{\pi k_i \mathbf{E} c_{k+2}}{2}.
\]

(B 2)

Here, \( \mathbf{E} \) is the identity matrix and \( A \) and \( B \) are \( (M_n + 1) \times (M_n + 1) \) matrices defined by

\[
A_{n,n'+1} = -n \gamma \delta_{n,n'}
\]

(B 3)

and

\[
B_{n,n'+1} = \left\{ \begin{array}{ll}
\alpha^2 + 2 D_s \left( n + \frac{1}{2} \right) & \delta_{n,n'} + 2 \alpha \sqrt{D_s n} \delta_{n-1,n'} \\
+ 2 \alpha \sqrt{D_s (n + 1)} \delta_{n+1,n'} & \\
& + \alpha \sqrt{n(n - 1)} \delta_{n-2,n'} \\
& + D_s \sqrt{(n + 1)(n + 2)} \delta_{n+2,n'}
\end{array} \right.
\]

(B 4)

where \( 0 \leq n \leq M_n \) and \( 0 \leq n' \leq M_n \). Introducing \( c_k = (c_{2k}^\top, c_{2k+1}^\top)^\top \) [58], equation (B 2), which is an equation with second-nearest-neighbour coupling,
reduces to the following equation with first-nearest-neighbour coupling:

\[ 0 = Q_k \tilde{c}_{k-1} + Q_k \tilde{c}_k + Q_k^* \tilde{c}_{k+1}, \quad (B5) \]

where \( Q_k \) are \((2M_k + 2) \times (2M_k + 2)\) matrices consisting of submatrices \( A \) and \( B \):

\[ Q_k = \begin{pmatrix} \pi k i E & 2k i E \\ 2(2k+1)iE & \pi(2k+1)iE \end{pmatrix} . \quad (B6) \]

\[ Q_k^* = \begin{pmatrix} \pi k i E & 0 \\ 0 & \pi(2k+1)iE \end{pmatrix} . \quad (B7) \]

We solve the recurrence relation for equation (B5) by introducing \( S_k \) and \( R_k \) that satisfy \( \tilde{c}_{k-1} = S_k \tilde{c}_k \) \((k \geq 0)\) and \( \tilde{c}_{k+1} = R_{k-1} \tilde{c}_k \) \((k \leq 0)\). With \( S_k \) and \( R_k \), equation (B5) is calculated as

\[ S_{k-1} = -[Q_k + Q_k^* S_k]^{-1} Q_k^* \tilde{c}_k, \quad (B9) \]

and

\[ R_k = -(Q_k R_{k-1} + Q_k)^{-1} Q_k^* \tilde{c}_k, \quad (B10) \]

where \( S_k \) and \( R_k \) can be obtained by truncating at large \( k \), namely at \( k = -\tilde{M}_k \). For \( k = 0 \), we have

\[ 0 = [Q_0^* R_{-1} + Q_0 + Q_0^* S_0] \tilde{c}_0, \quad (B11) \]

where the first row of the left part of the matrix in equation (B11) vanishes due to equations (B16)−(B8). Therefore, \( \tilde{c}_0 \) has a non-trivial solution and \( \tilde{c}_k \) can be calculated by recursively applying \( S_k \) and \( R_k \) to \( \tilde{c}_0 \).

REFERENCES


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