Physical insight into the thermodynamic uncertainty relation using Brownian motion in tilted periodic potentials

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Using Brownian motion in periodic potentials V(x) tilted by a force f, we provide physical insight into the thermodynamic uncertainty relation, a recently conjectured principle for statistical errors and irreversible heat dissipation in nonequilibrium steady states. According to the relation, nonequilibrium output generated from dissipative processes necessarily incurs an energetic cost or heat dissipation q, and in order to limit the output fluctuation within a relative uncertainty ϵ , at least $2k_BT/\epsilon^2$ of heat must be dissipated. Our model shows that this bound is attained not only at near-equilibrium $[f \ll V'(x)]$ but also at far-from-equilibrium $[f \gg V'(x)]$, more generally when the dissipated heat is normally distributed. Furthermore, the energetic cost is maximized near the critical force when the barrier separating the potential wells is about to vanish and the fluctuation of Brownian particles is maximized. These findings indicate that the deviation of heat distribution from Gaussianity gives rise to the inequality of the uncertainty relation, further clarifying the meaning of the uncertainty relation. Our derivation of the uncertainty relation also recognizes a bound of nonequilibrium fluctuations that the variance of dissipated heat (σ_q^2) increases with its mean (μ_q) , and it cannot be smaller than $2k_BT\mu_q$.

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I. INTRODUCTION

Precise determination of output information from a thermodynamically dissipative process necessarily incurs energetic cost to generate it. Tradeoffs between energetic cost and information processing in biochemical and biomolecular processes have been highlighted for the past few decades [1–5]. Among others, Barato and Seifert [1] have recently conjectured a fundamental bound in the minimal heat dissipation (q) to generate an output with relative uncertainty (ϵ) . To be specific, when a molecular motor moves along a cytoskeletal filament [6–8], the chemical free energy transduced into the motor movement, which results in a travel distance of X(t), is eventually dissipated as heat into the surrounding media [9,10], the amount of which increases with the time $(\langle q \rangle \sim t)$.

Because of the inherent stochasticity of chemical processes, the travel distance X(t) has its own variance, $\sigma_X^2 = \langle [\delta X(t)]^2 \rangle$, and it defines a time-dependent fluctuation in the output $\epsilon_X (\equiv \sigma_X/\mu_X)$, whose squared quantity decreases with time t, as $\epsilon_X^2 \sim t^{-1}$. The product of the two quantities, \mathcal{Q} , is in fact independent of t [1,11], and it was further argued that \mathcal{Q} is always greater than $2k_BT$ for any process that can be described as a Markov jump process on a suitable network. This notion is concisely written as

$$Q = \langle q \rangle \times \epsilon_X^2 \geqslant 2k_B T. \tag{1}$$

The validity of this inequality was claimed for general Markovian networks [1,2], and it was partly proved near equilibrium in the linear-response regime [1]. This effort has recently been followed by a general proof employing the large deviation theory [12–14].

Here, while limited to a particular model, we provide a less abstract and physically more tangible proof of the thermodynamic uncertainty relation [Eq. (1)] than the existing studies by considering the dynamics of a Brownian particle on a static

periodic potential subjected to a nonconservative force f. Projection of biomolecular processes in one-dimensional (1D) periodic potentials is fully legitimate as long as the time-scale separation between a slow variable of interest and other faster variables is ensured [15], and Brownian motion in a 1D periodic potential has routinely been employed in describing the motion of molecular motors and enzyme turnover reactions [7,10,16]. We directly calculate each term $(\langle q \rangle$ and $\epsilon_X^2)$ in Eq. (1), and we show that the product of the two quantities must be greater than $2k_BT$.

II. BROWNIAN MOTION IN TILTED PERIODIC POTENTIALS

The overdamped Langevin equation for the "position" x(t) of a quasiparticle on a periodic potential V(x) = V(x + L) is written as

$$\dot{x}(t) = \mu F(x(t), f) + \eta(t), \tag{2}$$

where μ is the motility coefficient (or inverse of friction coefficient $\gamma, \mu = \gamma^{-1}$), $F(x(t), f) \equiv -V'(x(t)) + f$, and Gaussian white noise is assumed such that $\langle \eta(t) \rangle = 0$ and $\langle \eta(t) \eta(t') \rangle = 2D\delta(t-t')$ with the diffusion constant $D = \mu k_B T$. Then, the corresponding Fokker-Planck equation for the probability density $\rho(x,t)$ is

$$\partial_t \rho(x,t) = D \partial_x [\partial_x - \beta F(x(t))] \rho(x,t)$$

= $-\partial_x j(x,t)$, (3)

which defines the probability current $j(x,t) = -D\partial_x \rho(x,t) + \mu F(x(t))\rho(x,t)$.

Equations (2) and (3) represent the Brownian motion in tilted washboard potentials where the extent of tilt is controlled by f [17]. At steady state, the probability density becomes time-independent $[\rho(x,t) = \rho_{ss}(x)]$, which in turn renders a constant probability current, $j(x,t) = j_{ss}$. Furthermore, heat (housekeeping heat [18–20]) has to be continuously dissipated to sustain the process at nonequilibrium steady state (NESS).

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Before carrying out an explicit calculation, two limiting cases are worth considering: (i) At weak tilt $[0 \lesssim f \ll V'(x)]$, it is expected that the particle hops stochastically between the adjacent confining potential wells of V(x) with a mean hopping time $\langle \tau \rangle$ and a small downhill velocity $\sim L/\langle \tau \rangle$ and a reduced effective diffusion constant $D_{\rm eff}(< D)$ [21,22]. (ii) At strong tilt $[f \gg V'(x)]$, the barrier separating the adjacent potentials vanishes, and the particles will drift downhill with mean steady-state velocity $v_{\rm ss} \sim \mu f$ and with the original diffusion constant D.

III. EVALUATION OF Q IN TILTED PERIODIC POTENTIALS

Here, our aim is to evaluate Q for arbitrary values of f and prove that Q is lower bounded by $2k_BT$. First, the heat dissipated from this process in NESS is a housekeeping heat, which can be evaluated for Langevin systems as [1,19,20]

$$q[x(t), f] = \mu^{-1} \int_0^t d\tau \, v_{ss}(x, f) \dot{x}(\tau), \tag{4}$$

where $v_{ss}(x, f) \equiv j_{ss}(f)/\rho_{ss}(x, f) = \mu F(x, f) - D\partial_x \log \rho_{ss}(x, f)$ is the mean local velocity. Note that due to the stochastic term $\dot{x}(\tau)$, the housekeeping heat is a stochastic quantity that depends on the path of realization. The argument [x(t)] of q makes it explicit that the calculated heat is for a particular realization of the trajectory $[x(t)] = (x(0), x(1), x(2), \dots, x(t))$, hence the housekeeping heat averaged over the ensemble of trajectories is written in the following form:

$$\langle q \rangle = \int dx_0 p(x_0) \int \prod_{i=1}^{t-1} dx_i P(x_i | x_{i-1}) q(x_0, \dots, x_t)$$

$$= \int \mathcal{D}[x(\tau)] e^{-S[x(\tau)|x_0]} \int_0^t d\tau \ \mu^{-1} v_{ss}(x(\tau)) \dot{x}(\tau)$$

$$= \left\langle \int_0^t d\tau \ v_{ss}(x(\tau)) F(x(\tau)) \right\rangle$$

$$= \langle v_{ss}(x, f) F(x, f) \rangle t \equiv \langle v F \rangle_{ss} t, \tag{5}$$

where $S[x(\tau),f(\tau)]=\int_0^t d\tau (\frac{[\dot{x}-\mu F(x,f)]^2}{4D}+\frac{\mu}{2}\partial_x F)$ [20], and $\langle\cdots\rangle\equiv\int \mathcal{D}[x(\tau)]e^{-S[x(\tau)|x_0]}(\cdots)$ denotes the average over all the paths and initial conditions. At steady state, however, the implicit time dependence in $v_{\rm ss}(x(\tau))$ and $F(x(\tau))$ can be removed from the above formal path integral expression, and thus the notion of a sum over all paths is replaced with an integral weighed with the steady-state probability, $\rho_{\rm ss}(x)$, with a normalization condition, $\int_0^L \rho_{\rm ss}(x) dx = 1$. That is, $\langle g \rangle = \int \mathcal{D}(x(\tau))P[x(\tau)|x_0]\int_0^t d\tau g(x(\tau)) = \int dx g(x)\rho_{\rm ss}(x)$. In the last line of Eq. (5), we have dropped the dependence of steady-state quantities on x and f from the expression and used a simplified notation $\langle\cdots\rangle_{\rm ss}$. Henceforth, for notational convenience, we will use this simplified notation, i.e., $\langle K\rangle_{\rm ss} \equiv \langle K_{\rm ss}(x,f)\rangle = \int_0^L K_{\rm ss}(x,f)\rho_{\rm ss}(x,f)dx$. Next, the mean travel distance $\langle X(t)\rangle$ and its variance

Next, the mean travel distance $\langle X(t) \rangle$ and its variance $(\langle [\delta X(t)]^2 \rangle)$ of Brownian motion in tilted periodic potentials are a topic that has been discussed in many different contexts, and their analytic forms at $t \to \infty$ are available from

Refs. [23-25],

$$\langle X(t) \rangle = \mu \left\langle \int_0^t d\tau \ F[x(\tau), f] \right\rangle = \mu \langle F \rangle_{ss} t$$
 (6)

and

$$\langle [\delta X(t)]^2 \rangle = 2D_{\text{eff}}(f)t, \tag{7}$$

where $D_{\text{eff}}(f) = D\mathcal{G}(f)$ is a force-dependent effective diffusion coefficient,

$$\mathcal{G}(f) = \frac{\langle I_{\mp}(x,f)I_{+}(x,f)I_{-}(x,f)\rangle_{L}}{\langle I_{\mp}(x,f)\rangle_{L}^{3}},\tag{8}$$

where $\langle \cdots \rangle_L \equiv L^{-1} \int_0^L (\cdots) dx$ denotes averaging over a period with

$$I_{+}(x,f) = e^{\beta \Phi(x,f)} \int_{x-L}^{x} dy \, e^{-\beta \Phi(y,f)}$$
 (9)

and

$$I_{-}(x,f) = e^{-\beta\Phi(x,f)} \int_{x}^{x+L} dy \, e^{\beta\Phi(y,f)},$$
 (10)

where $\Phi(x, f) \equiv V(x) - fx$.

Now, we are ready to evaluate Q [Eq. (1)] using Eqs. (5)–(7), and we prove the uncertainty relation, $Q \ge 2k_BT$,

$$Q = \langle q \rangle \times \frac{\langle [\delta X(t)]^2 \rangle}{\langle X(t) \rangle^2}$$

$$= 2k_B T \frac{\langle vF \rangle_{ss}}{\mu \langle F \rangle_{ss}^2} \mathcal{G}(f). \tag{11}$$

The two core averages in Eq. (11) are evaluated as follows:

$$\langle F \rangle_{ss} = \int_0^L F(x) \rho_{ss}(x) dx$$

$$= \int_0^L [\gamma j_{ss}(f) + k_B T \partial_x \rho_{ss}(x, f)] dx = \gamma j_{ss}(f) L$$
(12)

and

$$\langle vF \rangle_{ss} = \int_0^L v_{ss}(x) F(x) \rho_{ss}(x) dx$$

$$= \int_0^L v_{ss}(x, f) [\gamma j_{ss}(f) + k_B T \partial_x \rho_{ss}(x, f)] dx$$

$$= \gamma j_{ss}^2(f) \int_0^L \rho_{ss}^{-1}(x, f) dx, \qquad (13)$$

where the condition of periodic boundary $\rho_{ss}(L) = \rho_{ss}(0)$ was used in both Eqs. (12) and (13). Now, to prove the uncertainty relation, we have to verify the following inequality for all f:

$$\frac{\mathcal{Q}(f)}{2k_BT} = \left(\frac{1}{L^2} \int_0^L \rho_{\rm ss}^{-1}(x, f) dx\right) \times \mathcal{G}(f) \geqslant 1. \tag{14}$$

The conditions of normalization $\int_0^L \rho_{ss}(x,f) dx = 1$ and boundedness $|\rho_{ss}(x,f)| < \infty$ for all x's enable us to calculate the position-dependent steady-state probability $\rho_{ss}(x,f)$ and steady-state current $j_{ss}(f)$ [17] (see Appendix A), both of

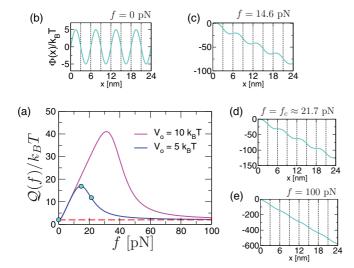


FIG. 1. Q(f) calculated for $\Phi(x, f) = V(x) - fx$ with $V(x) = V_o \sin(2\pi x/L)$, $V_o = 5 k_B T$, and L = 6 nm [blue line in panel (a)]. The shapes of the potential $\Phi(x, f)$ at varying f are shown in the small panels (b)–(e). A greater dissipation [larger Q(f)] is obtained for a deeper potential well $(V_o = 10 k_B T)$, magenta line). The red dashed line depicts the lower bound $Q = 2k_B T$.

which are required for evaluating Q explicitly,

$$\rho_{ss}(x,f) = \frac{j_{ss}(f)e^{-\beta\Phi(x,f)}}{D\Omega(\beta f L)} [\psi_{+}(L,f) - \Omega(\beta f L)\psi_{+}(x,f)], \quad (15)$$

$$j_{ss}(f) = \frac{D\Omega(\beta f L)}{\psi_{+}(L, f)\psi_{-}(L, f) - \Omega(\beta f L)\Psi_{+}(L, f)}, \quad (16)$$

where $\Psi_+(L,f) = \int_0^L dx \, e^{-\beta \Phi(x,f)} \psi_+(x,f)$, $\beta = 1/k_B T$, $\Omega(x) = 1 - e^{-x}$, and $\psi_\pm(x,f) = \int_0^x e^{\pm\beta \Phi(x',f)} dx'$. Insertion of Eqs. (A7) and (16) into $\langle F \rangle_{\rm ss}$ [Eq. (12)] and $\langle vF \rangle_{\rm ss}$ [Eq. (13)] allows us to calculate the f dependence of $\mathcal Q$, which is depicted in Fig. 1(a).

Three regimes of f are investigated: (i) In the weak tilt limit $[V'(x)\gg f\to 0]$, using Eqs. (12), (13), (A7), (16), and the periodicity of V(x), i.e., $\int_{x-L}^x e^{\pm\beta V(y)}dy=\int_0^L e^{\pm\beta V(y)}dy$, one can show that $\langle F\rangle_{\rm ss}\to f\varphi_+^{-1}\varphi_-^{-1}$, where $\varphi_\pm\equiv\langle e^{\pm\beta V(x)}\rangle_L$, $\langle vF\rangle_{\rm ss}\to \mu f^2\varphi_+^{-1}\varphi_-^{-1}$, and $\mathcal{G}(f)\to\varphi_+^{-1}\varphi_-^{-1}$, where $\varphi_\pm=\langle e^{\pm\beta V(x)}\rangle_L$. This leads to $\mathcal{Q}(f)/2k_BT\to 1$. A series expansion of $\mathcal{Q}(f)$ in the power of f leads to (see Appendix B 1 for the details of the power-series expansion)

$$\lim_{f \to 0 \leqslant V'(x)} \frac{\mathcal{Q}}{2k_B T} = 1 + \lambda \beta f + O(f^2) \geqslant 1$$
 (17)

with $\lambda \geqslant 0$ [Eq. (B20)]. (ii) In the strong tilt limit [$V'(x) \ll f$], the particle continuously drifts downhill without being trapped in potential wells. In this case, $\langle F \rangle_{ss} \to f$, $\langle vF \rangle_{ss} \to \mu f^2$, and $\mathcal{G}(f) \to 1$, which again leads to $\mathcal{Q}(f)/2k_BT \to 1$. A series expansion of $\mathcal{Q}(f)$ in the power of 1/f leads to (see Appendix B 2)

$$\lim_{V'(x)\ll f} \frac{\mathcal{Q}}{2k_B T} \geqslant 1 + 3\frac{\langle \{V'(x)\}^2 \rangle_L}{f^3} + \dots \geqslant 1.$$
 (18)

(iii) Figure 1 shows that Q(f) is maximized at an intermediate till limit $f \lesssim f_c$, which satisfies $V'(x) - f_c \approx 0$. In this case, $\Phi(x, f)$ resembles a descending staircase (see Fig. 1 at $f \approx f_c$). It is straightforward to show that (see Appendix B 3)

$$\frac{Q(f_c)}{2k_B T} \simeq \frac{\beta f_c L}{3} \frac{(1 + 5e^{-\beta f_c L} + 5e^{-2\beta f_c L} + e^{-3\beta f_c L})}{(1 + e^{-\beta f_c L})^2 (1 - e^{-\beta f_c L})}
\geqslant 1,$$
(19)

where $Q(f_c)$ increases monotonically with f_c and the equality is attained only for $f_c L \ll k_B T$, which is realized essentially for a barrierless, flat potential.

Taking (i)–(iii) together, we have essentially proved that $\mathcal{Q}(f)/2k_BT \geqslant 1$ for all f. Remarkably, the lower bound of $\mathcal{Q}, 2k_BT$, is attained at the two disparate conditions of f, and it is of particular significance that \mathcal{Q} is maximized near the critical force $(f \lesssim f_c)$ at which the barrier of the potential is about to vanish and the fluctuation of the Brownian particles is maximized.

IV. THERMODYNAMIC UNCERTAINTY RELATION AND HEAT DISTRIBUTION

Instead of the travel distance X(t) as an output observable, the dissipated heat (q) in steady state can be used as an alternative probe of output from the process. For a given thermodynamic affinity per cycle \mathcal{A} , which itself is a deterministic quantity defined as the log-ratio between the forward and backward flux (or microscopic rate constants of chemical networks) [1,10,26], the mean and variance of the housekeeping heat can be related with those of another stochastic observable, such as reaction cycle step n(t) or travel distance X(t): $\langle q \rangle = \mathcal{A} \times \langle n \rangle = \mathcal{A}/L \times \langle X \rangle$ and $\langle (\delta q)^2 \rangle = \mathcal{A}^2 \times \langle (\delta n)^2 \rangle = (\mathcal{A}/L)^2 \times \langle (\delta X)^2 \rangle$. Then, the squared uncertainty $\epsilon_{\xi}^2 = \sigma_{\xi}^2/\mu_{\xi}^2$ is identical for $\xi = q(t), n(t)$, and X(t).

If the dissipated heat itself is used as an output observable $(\xi = q)$, \mathcal{Q} turns into a Fano factor of q and is lower bounded by $2k_BT$,

$$Q = \mu_q \times \epsilon_q^2 = \sigma_q^2 / \mu_q \geqslant 2k_B T, \tag{20}$$

or equivalently,

$$0 \leqslant \mu_q \leqslant \frac{\sigma_q^2}{2k_B T}. (21)$$

The lower bound of μ_q is a straightforward outcome of the second law of the thermodynamics, but the upper bound, which is an interesting outcome, implies that the variance of heat dissipated in NESS is constrained by its mean, such that σ_q^2 grows with μ_q and cannot be smaller than $2k_BT \times \mu_q$. While the thermodynamic uncertainty relation has originally recognized the bound of steady-state current fluctuation (ϵ_J) [12], here we show that the relation of variance of heat dissipation with its mean [Eq. (21)] can be deduced from it as well.

Next, we relate Eqs. (20) and (21) with the integral fluctuation theorem for housekeeping heat, $\langle e^{-\beta q} \rangle = 1$ [27]. The first inequality in Eq. (21) $(0 \le \mu_q)$ is obtained from Jensen's inequality for convex functions, $\langle e^{-\beta q} \rangle \ge e^{-\beta \langle q \rangle}$, and the second one $(\mu_q \le \sigma_1^2/2k_BT)$ is obtained by truncating the

cumulant expansion of $e^{-\beta q}$ at the second term as

$$0 = -\beta^{-1} \log \langle e^{-\beta q} \rangle$$

$$= \mu_q - \frac{\beta}{2} \sigma_q^2 + \mathcal{R}(\beta q) \geqslant \mu_q - \frac{\beta}{2} \sigma_q^2, \qquad (22)$$

and by claiming that the remaining sum of alternating series beyond the second cumulant is non-negative regardless of the value of βq , i.e., $\mathcal{R}(\beta q) \ge 0$. To be consistent with the form of the thermodynamic uncertainty relation in Eq. (20), the inequality $\mathcal{R}(\beta q) \ge 0$ should hold. The equality sign is acquired when the heat distribution, P(q), is Gaussian.

Speck et al. [27], in fact, have calculated P(q,t) by solving the Fokker-Planck equation of Brownian motion in periodic potentials through adiabatic elimination of fast variables. They found that the dissipated heat in steady states takes a form of Gaussian distribution $P(q,t) \sim \exp[-(q-\mu_q)^2/2\sigma_q^2]$ at two limiting cases. For $|V'(x)| \gg f$,

$$P(q,t) \sim \exp\left[-\frac{(q - \gamma \langle v^2 \rangle_{ss} t)^2}{4\gamma k_B T \langle v^2 \rangle_{ss} t}\right],$$
 (23)

which gives $\mu_q = \gamma \langle v^2 \rangle_{\rm ss} t$, $\sigma_q^2 = 2 \gamma k_B T \langle v^2 \rangle_{\rm ss} t$, and Q = $\sigma_a^2/\mu_q = 2k_BT$. For $|V'(x)| \ll f$,

$$P(q,t) \sim \exp\left[-\frac{(q-\mu f^2 t)^2}{4Df^2 t}\right],$$
 (24)

which gives $\mu_q = \mu f^2 t$ and $\sigma_q^2 = 2Df^2 t$. In both cases, $\mathcal{Q} =$ $\sigma_q^2/\mu_q = 2k_BT$. These results (i) agree with those shown in Eqs. (17) and (18), which use the travel distance as an output $(Q = \mu_q \epsilon_X^2 = 2k_B T)$, (ii) confirm that Q is time-independent, and (iii) confirm that Gaussian dissipation leads to $Q = 2k_BT$, as we have discussed using the integral fluctuation theorem [Eq. (22)].

V. CONCLUSIONS

The implication of the thermodynamic uncertainty relation, which differs from other inequality relations such as the second law and the stability condition in equilibrium thermodynamics [28], is worth further deliberation. It is interesting that the lower bound of Q is attained both near and far from equilibrium. For a unicyclic Markovian network with N states, it was shown that $Q \ge (A/N) \coth(A/2Nk_BT) \ge 2k_BT$ [1]. In this case, the minimum dissipation bound of $Q = 2k_BT$ is attained only when the affinity goes to zero $(A \rightarrow 0)$, in which the local detailed balance condition is approached. Our

limiting case of $f \gg V'(x)$ could be thought of as $A \gg 1$, but the above expression of Q from the Markovian network diverges as $A \gg 1$ at fixed N, which appears to contradict Eq. (18). Under the condition of $f \gg V'(x)$, however, the potential barriers between adjacent wells vanish and the mapping of dissipative dynamics using the Markov jump process on networks can no longer be maintained. While the condition is fundamentally different from another limiting case near equilibrium, we still find the $Q = 2k_BT$ bound being attained at this extreme driving condition that also gives rise to a Gaussian heat dissipation, a hallmark of independence and uncorrelated statistics. Also suggested in Fig. 1, except for the two limiting conditions, it is likely that the distribution of dissipated heat is characterized by non-Gaussianity. Thus, Q, greater than $2k_BT$, implies deviation of heat dissipation from Gaussian, and it can be used as a measure for assessing the complexity of dissipative processes, which, for the case of Brownian motion in 1D periodic potentials, approaches its lower bound both near and far from equilibrium.

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APPENDIX A: DERIVATION OF $\rho_{ss}(x, f)$ AND $j_{ss}(f)$ [17]

The Fokker-Planck equation with effective potential $\Phi(x, f) = V(x) - fx$ is

$$\partial_t \rho(x, f, t) = D \partial_x [\partial_x + \beta \Phi'(x; f)] \rho(x, t)$$

= $-\partial_x j(x, f, t)$. (A1)

At steady state, $\rho(x, f, t) = \rho_{ss}(x, f)$ and $j(x, f, t) = j_{ss}(f)$,

$$j_{ss}(f) = -D\partial_x \rho_{ss}(x, f) - \mu \Phi'(x) \rho_{ss}(x, f)$$

= $-De^{-\beta \Phi(x, f)} \partial_x [e^{\beta \Phi(x, f)} \rho_{ss}(x, f)].$ (A2)

Here, $\rho_{ss}(x, f)$ can be formally solved as

$$\rho_{ss}(x,f) = Ne^{-\beta\Phi(x,f)} - \frac{j_{ss}(f)}{D}e^{-\beta\Phi(x,f)} \int_{-\infty}^{x} e^{\beta\Phi(y,f)} dy$$
(A3)

and one can determine N, the normalization constant, by using the fact that the steady-state probability $\rho_{ss}(x)$ is bounded for large x and j_{ss} by using $\int_0^L \rho_{ss}(x) dx = 1$. To carry out this algebra, let us first evaluate

$$\int_{0}^{x+nL} e^{\beta \Phi(x')} dx' = \int_{0}^{L} e^{\beta \Phi(x')} dx' + \dots + \int_{(n-1)L}^{nL} e^{\beta \Phi(x')} dx' + \int_{nL}^{nL+x} e^{\beta \Phi(x')} dx'
= (1 + e^{-\beta f L} + \dots + e^{-\beta f (n-1)}) \int_{0}^{L} e^{\beta \Phi(x')} dx' + e^{-\beta f n L} \int_{0}^{x} e^{\beta \Phi(x')} dx'
= \frac{1 - e^{-\beta f n L}}{1 - e^{-\beta f L}} I + e^{-\beta f n L} \int_{0}^{x} dx' e^{\beta V(x')}, \tag{A4}$$

where $I \equiv \int_0^L e^{\beta \Phi(x')} dx'$. This allows us to express $\rho_{\rm ss}(x+nL)$ as

$$\rho_{ss}(x+nL) = e^{-\beta\Phi(x+nL)} \left(N - \frac{j_{ss}}{D} \int_{0}^{x+nL} e^{\beta\Phi(x')} dx' \right)
= e^{-\beta\Phi(x,f)} e^{\beta f n L} \left[N - \frac{j_{ss}}{D} \left(I \frac{1 - e^{-\beta f n L}}{1 - e^{-\beta f L}} + e^{-\beta f n L} \int_{0}^{x} dx' e^{\beta V(x')} \right) \right]
= e^{-\beta\Phi(x,f)} e^{\beta f n L} \left[N - \frac{j_{ss}I}{D(1 - e^{-\beta f L})} \right] + e^{-\beta\Phi(x,f)} \left(\frac{j_{ss}I}{D} \frac{1}{1 - e^{-\beta f L}} - \frac{j_{ss}}{D} \int_{0}^{x} dx' e^{\beta V(x')} \right). \tag{A5}$$

In order for $\rho_{ss}(x+nL)$ to be bounded even when $n\to\infty$ (f>0), the first term in the last line of Eq. (A5) should vanish, which demands

$$N = \frac{j_{\rm ss}I}{D(1 - e^{-\beta fL})}. (A6)$$

Therefore, the steady-state probability along the reaction coordinate is written as

$$\rho_{ss}(x) = \frac{j_{ss}}{D} e^{-\beta \Phi(x,f)} \left(\frac{\psi_{+}(L)}{1 - e^{-\beta fL}} - \psi_{+}(x) \right), \tag{A7}$$

where $\psi_{\pm}(x) = \int_0^x e^{\pm\beta\Phi(x')} dx'$.

Next, the normalization condition $\int_0^L \rho_{ss}(x, f) dx = 1$ determines $j_{ss}(f)$

$$j_{ss}(f) = \frac{D(1 - e^{-\beta f L})}{\psi_{+}(L, f)\psi_{-}(L, f) - (1 - e^{-\beta f L}) \int_{0}^{L} dx \, e^{-\beta \Phi(x, f)} \psi_{+}(x, f)}.$$
(A8)

APPENDIX B: BEHAVIORS OF Q(f) AT THREE REGIMES OF f [23–25]

For three different regimes of f, we will evaluate

$$\frac{Q(f)}{2k_BT} = \frac{1}{L^2} \int_0^L dx \, \rho_{ss}(x, f) \times \frac{\langle [I_-(x, f)]^2 I_+(x, f) \rangle_L}{\langle I_-(x, f) \rangle_L^3}.$$
 (B1)

To evaluate Eq. (B1), it is convenient to have the following four identities [23–25]: First,

$$I_{+}(x,f) = e^{\beta \Phi(x,f)} \int_{x-L}^{x} dy \, e^{-\beta \Phi(y,f)} = \int_{0}^{L} dy \, e^{\beta [\Phi(x,f) - \Phi(x-y,f)]} = \int_{0}^{L} dy \, e^{\beta [V(x) - V(x-y)]} e^{-\beta fy}. \tag{B2}$$

Second,

$$I_{-}(x,f) = e^{-\beta\Phi(x,f)} \int_{x}^{x+L} dy \, e^{\beta\Phi(y,f)} = \int_{0}^{L} dy \, e^{-\beta[\Phi(x,f)-\Phi(x+y,f)]} = \int_{0}^{L} dy \, e^{-\beta[V(x)-V(x+y)]} e^{-\beta fy}. \tag{B3}$$

Third,

$$\frac{1}{L} \int_{0}^{L} dx \int_{0}^{L} dy \, y e^{-\beta[V(x) + V(x - y)]} = \frac{1}{L} \int_{0}^{L} dx \int_{0}^{L} dy (L - y) e^{-\beta[V(x) + V(x + y)]}$$

$$= L \varphi_{-}^{2} - \frac{1}{L} \int_{0}^{L} dx \int_{0}^{L} dy \, y e^{-\beta[V(x) + V(x + y)]}$$

$$= L \varphi_{-}^{2} - \frac{1}{L} \int_{0}^{L} dx \int_{0}^{L} dy \, y e^{-\beta[V(x - y) + V(x)]}, \tag{B4}$$

which leads to

$$\frac{1}{L} \int_0^L dx \int_0^L dy \, y e^{-\beta[V(x-y) + V(x)]} = \frac{L\varphi_-^2}{2}.$$
 (B5)

Lastly,

$$l_o^2 = \frac{1}{L} \int_0^L dx \, e^{-\beta V(x)} \underbrace{\int_0^L dy \, y e^{\beta V(x+y)}}_{\int_x^{L+x} ds (s-x) e^{\beta V(s)}} = \frac{1}{L} \int_0^L dx \, e^{-\beta V(x)} [L\langle x \rangle_+ + L\psi_+(x,0) - xL\varphi_+]$$

$$= L\langle x \rangle_+ \varphi_- - L\langle x \rangle_- \varphi_+ + \Psi_+(L,0), \tag{B6}$$

where $\langle x^n \rangle_{\pm} \equiv \frac{1}{L} \int_0^L dx \, x^n e^{\pm \beta V(x)}$ and $\Psi_+(x,f) = \int_0^x dy \, e^{-[\beta V(y) - fy]} \int_0^y dz \, e^{\beta [V(z) - fz]}$, thus $\Psi_+(L,0) = \int_0^L dx \, e^{-\beta V(x)} \int_0^x dx \, e^{\beta V(x)}$.

1. Weak tilt limit, $V'(x) \gg f$

First,

$$I_{-}(x,f) = \int_{0}^{L} dy \, e^{-\beta[V(x) - V(x+y)]} (1 - \beta f y + \cdots) = e^{-\beta V(x)} \int_{0}^{L} dy \, e^{\beta V(y)} - \beta f \int_{0}^{L} dy \, y e^{-\beta[V(x) - V(x+y)]} + O(f^{2}), \quad (B7)$$

where we have used a property of periodic function, $\int_0^L dy \, e^{\beta V(x+y)} = \int_0^L dy \, e^{\beta V(y)}$. Then, the average over a period is

$$\langle I_{-}(x,f)\rangle_{L} = \frac{1}{L} \underbrace{\int_{0}^{L} dx \, e^{-\beta V(x)}}_{=L\varphi_{-}} \underbrace{\int_{0}^{L} dy \, e^{\beta V(y)}}_{=L\varphi_{+}} - \beta f \underbrace{\frac{1}{L} \int_{0}^{L} dx \int_{0}^{L} dy \, y e^{-\beta [V(x) - V(x+y)]}}_{=l_{o}^{2}} + O(f^{2})$$

$$= L\varphi_{+}\varphi_{-} \left(1 - \frac{l_{o}^{2} \beta f}{L\varphi_{+}\varphi_{-}} + O(f^{2})\right), \tag{B8}$$

where $\varphi_{\pm} = \frac{1}{L} \int_0^L dx \ e^{\pm \beta V(x)}$ and $l_o^2 = \frac{1}{L} \int_0^L dx \ e^{-\beta V(x)} \int_0^L dy \ y e^{\beta V(x+y)}$. Hence, we obtain

$$\langle I_{-}(x,f)\rangle_{L}^{3} = L^{3}\varphi_{+}^{3}\varphi_{-}^{3}\left(1 - \frac{3l_{o}^{2}}{L\varphi_{+}\varphi_{-}}\beta f + O(f^{2})\right).$$
(B9)

Next,

$$\langle [I_{-}(x,f)]^{2}I_{+}(x,f)\rangle_{L} = \frac{1}{L} \int_{0}^{L} dx [I_{-}(x)]^{2} \left[\int_{0}^{L} dy \, e^{\beta[V(x)-V(x-y)]} e^{-\beta fy} \right]$$

$$= \frac{1}{L} \int_{0}^{L} dx \, e^{-\beta V(x)} \left(L^{2} \varphi_{+}^{2} - 2L \varphi_{+} \int_{0}^{L} dy \, y e^{\beta V(x+y)} \beta f + \cdots \right)$$

$$\times \left(\int_{0}^{L} dy \, e^{-\beta V(x-y)} - \beta f \int_{0}^{L} dy \, y e^{-\beta V(x-y)} + \cdots \right)$$

$$= \underbrace{\frac{1}{L} \int_{0}^{L} dx \, e^{-\beta V(x)}}_{=L\varphi_{-}} L^{3} \varphi_{+}^{2} \varphi_{-} - 2\beta f L^{2} \varphi_{+} \varphi_{-} \underbrace{\frac{1}{L} \int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{L} dy \, y e^{\beta V(x+y)}}_{=l^{2}}$$

$$- \beta f L^{2} \varphi_{+}^{2} \underbrace{\frac{1}{L} \int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{L} dy \, y e^{-\beta V(x-y)}}_{=L^{2} \varphi_{-}^{2}/2} \underbrace{[Eq. (B5)]}_{L\varphi_{-}, \varphi_{-}}$$

$$= L^{3} \varphi_{+}^{2} \varphi_{-}^{2} \left(1 - \frac{2l_{o}^{2} + L^{2} \varphi_{+} \varphi_{-}/2}{L \varphi_{-}, \varphi_{-}} \beta f + O(f^{2}) \right). \tag{B10}$$

Therefore,

$$\frac{\langle [I_{-}(x,f)]^2 I_{+}(x,f) \rangle_L}{\langle I_{-}(x,f) \rangle_L^3} = \frac{1}{\varphi_{+}\varphi_{-}} \left[1 + \left(\frac{l_o^2}{L^2 \varphi_{+} \varphi_{-}} - \frac{1}{2} \right) \beta f L + O(f^2) \right]. \tag{B11}$$

Lastly,

$$\frac{1}{L^2} \int_0^L \rho_{\rm ss}^{-1}(x,f) dx = \frac{1}{L^2} \int_0^L dx \frac{e^{\beta \Phi(x,f)} [\psi_+(L,f)\psi_-(L,f) - \Omega(\beta f L)\psi_+(x,f)]}{\psi_+(L,f) - \Omega(\beta f L)\psi_+(x,f)} = \frac{1}{L^2} \int_0^L dx \, e^{\beta \Phi(x,f)} \frac{\mathcal{N}(x,f)}{\mathcal{D}(x,f)}, \quad (B12)$$

where $\Psi_+(x,f) = \int_0^x dy \, e^{-\beta \Phi(y,f)} \psi_+(y,f) = \int_0^x dy \, e^{-\beta \Phi(y,f)} \int_0^y dz \, e^{\beta \Phi(z,f)}$. For small $f[f \ll V'(x)]$,

$$\psi_{\pm}(L,f) = \int_0^L dx \, e^{\pm\beta\Phi(x,f)} = \int_0^L dx \, e^{\pm\beta V(x)} (1 \mp \beta f x + \cdots) = L\varphi_{\pm} \mp (\beta f L) \langle x \rangle_{\pm} + \cdots$$
 (B13)

with $\langle x^n \rangle_{\pm} = \frac{1}{L} \int_0^L dx \, x^n e^{\pm \beta V(x)}$. Thus, one can expand the numerator and denominator defined, respectively, as $\mathcal{N}(x,f)$ and $\mathcal{D}(x,f)$ in Eq. (B12) in the power of f:

$$\mathcal{N}(x,f) = \psi_{+}(L,f)\psi_{-}(L,f) - \Omega(\beta f L)\Psi_{+}(x,f)$$

$$= [L\varphi_{+} - (\beta f L)\langle x\rangle_{+} + \cdots][L\varphi_{-} + (\beta f L)\langle x\rangle_{-} + \cdots] - \Omega(\beta f L)\Psi_{+}(x,f)$$

$$= L^{2}\varphi_{+}\varphi_{-} - [L\langle x\rangle_{+}\varphi_{-} - L\langle x\rangle_{-}\varphi_{+} + \Psi_{+}(x,0)](\beta f L) + O(f^{2})$$
(B14)

and

$$\mathcal{D}(x,f) = \psi_{+}(L,f) - \Omega(\beta f L)\psi_{+}(x,f) = L\varphi_{+} - [\langle x \rangle_{+} + \psi_{+}(x,0)]\beta f L + O(f^{2}). \tag{B15}$$

Equations (B12), (B14), and (B15) lead to the power-series expansion of $\frac{1}{L^2} \int_0^L \rho_{ss}^{-1}(x, f)$ in terms of f,

$$\frac{1}{L^{2}} \int_{0}^{L} dx \, \rho_{ss}^{-1}(x, f) = \frac{1}{L^{2}} \int_{0}^{L} dx \, e^{\beta \Phi(x, f)} \frac{\mathcal{N}(x, f)}{\mathcal{D}(x, f)}$$

$$= \frac{1}{L^{2}} \int_{0}^{L} dx \, e^{\beta V(x)} (1 - \beta f x + \cdots) \frac{L^{2} \varphi_{+} \varphi_{-} - [L\langle x \rangle_{+} \varphi_{-} - L\langle x \rangle_{-} \varphi_{+} + \Psi_{+}(x, 0)] (\beta f L) + \cdots}{L \varphi_{+} - [\langle x \rangle_{+} + \psi_{+}(x, 0)] \beta f L + \cdots}$$

$$\approx \varphi_{+} \varphi_{-} + \left[\langle x \rangle_{-} \varphi_{+} - \langle x \rangle_{+} \varphi_{-} + \frac{1}{L \varphi_{+}} \int_{0}^{L} dx \, e^{\beta V(x)} \left\{ \varphi_{-} \psi_{+}(x, 0) - \frac{\Psi_{+}(x, 0)}{L} \right\} \right] \beta f + O(f^{2})$$

$$= \varphi_{+} \varphi_{-} \left[1 + \left(\frac{\langle x \rangle_{-}}{\varphi_{-}} - \frac{\langle x \rangle_{+}}{\varphi_{+}} + \frac{1}{\varphi_{+}} \int_{0}^{L} dx \, e^{\beta V(x)} \left\{ \frac{\psi_{+}(x, 0)}{L \varphi_{+}} - \frac{\Psi_{+}(x, 0)}{L^{2} \varphi_{+} \varphi_{-}} \right\} \right) \beta f + O(f^{2}) \right]. \tag{B16}$$

Taken together,

$$\frac{Q(f)}{2k_{B}T} = \frac{1}{L^{2}} \int_{0}^{L} dx \, \rho_{ss}^{-1}(x) \times \frac{\langle [I_{-}(x)]^{2}I_{+}(x)\rangle_{L}}{\langle I_{-}(x)\rangle_{L}^{3}} \\
= \varphi_{+}\varphi_{-} \left[1 + \left(\frac{\langle x \rangle_{-}}{\varphi_{-}} - \frac{\langle x \rangle_{+}}{\varphi_{+}} + \frac{1}{\varphi_{+}} \int_{0}^{L} dx \, e^{\beta V(x)} \left\{ \frac{\psi_{+}(x,0)}{L\varphi_{+}} - \frac{\psi_{+}(x,0)}{L^{2}\varphi_{+}\varphi_{-}} \right\} \right) \beta f + O(f^{2}) \right] \\
\times \frac{1}{\varphi_{+}\varphi_{-}} \left[1 + \left(\frac{2l_{o}^{2} - L^{2}\varphi_{+}\varphi_{-}}{2L\varphi_{+}\varphi_{-}} \right) \beta f + O(f^{2}) \right] \\
= 1 + \left[\left(\frac{l_{o}^{2} - L^{2}\varphi_{+}\varphi_{-}/2 + L\langle x \rangle_{-}\varphi_{+} - L\langle x \rangle_{+}\varphi_{-}}{L\varphi_{+}\varphi_{-}} \right) + \frac{1}{\varphi_{+}} \int_{0}^{L} dx \, e^{\beta V(x)} \left\{ \frac{\psi_{+}(x,0)}{L\varphi_{+}} - \frac{\psi_{+}(x,0)}{L^{2}\varphi_{+}\varphi_{-}} \right\} \right] \beta f + \cdots \\
= 1 + \underbrace{\left[\left(\frac{\Psi_{+}(L,0) - L^{2}\varphi_{+}\varphi_{-}/2}{L\varphi_{+}\varphi_{-}} \right) + \frac{1}{\varphi_{+}} \int_{0}^{L} dx \, e^{\beta V(x)} \left\{ \frac{\psi_{+}(x,0)}{L\varphi_{+}} - \frac{\Psi_{+}(x,0)}{L^{2}\varphi_{+}\varphi_{-}} \right\} \right] \beta f + \cdots}_{-1} \right]}_{-1}$$
(B17)

Now, for $Q(f)/2k_BT \ge 1$ to be valid, the prefactor of βf , λ , should be non-negative, i.e., $\lambda \ge 0$,

$$\lambda = \frac{1}{\varphi_{+}} \left(\frac{\int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{x} dy \, e^{\beta V(y)}}{\int_{0}^{L} dx \, e^{-\beta V(x)}} - \frac{L\varphi_{+}}{2} + \frac{\int_{0}^{L} dx \, e^{\beta V(x)} \int_{0}^{x} dy \, e^{\beta V(y)}}{\int_{0}^{L} dx \, e^{\beta V(x)}} - \frac{\int_{0}^{L} dx \, e^{\beta V(x)} \left(\int_{0}^{x} dy \, e^{-\beta V(y)} \int_{0}^{y} dz \, e^{\beta V(z)} \right)}{\int_{0}^{L} dx \, e^{\beta V(x)} \int_{0}^{L} dx \, e^{-\beta V(x)}} \right). \tag{B18}$$

Because $\int_0^L dx \, e^{\beta V(x)} \int_0^x dy \, e^{\beta V(y)} = \frac{1}{2} (\int_0^L dx \, e^{\beta V(x)})^2 = \frac{L^2 \varphi_+^2}{2}$, the second and third terms in Eq. (B18) vanish. The numerator of the last term in Eq. (B18) can be rewritten as

$$\int_{0}^{L} dx \, e^{\beta V(x)} \int_{0}^{x} dy \, e^{-\beta V(y)} \int_{0}^{y} dz \, e^{\beta V(z)} = \int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{x} dy \, e^{\beta V(y)} \int_{x}^{L} dz \, e^{\beta V(z)}$$

$$\leq \int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{x} dy \, e^{\beta V(y)} \int_{0}^{L} dz \, e^{\beta V(z)}. \tag{B19}$$

Therefore, $\lambda \geqslant 0$ is further ensured from the following:

$$\lambda = \frac{1}{\varphi_{+}} \left(\frac{\int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{x} dy \, e^{\beta V(y)}}{\int_{0}^{L} dx \, e^{-\beta V(x)}} - \frac{\int_{0}^{L} dx \, e^{\beta V(x)} \left(\int_{0}^{x} dy \, e^{-\beta V(y)} \int_{0}^{y} dz \, e^{\beta V(z)} \right)}{\int_{0}^{L} dx \, e^{-\beta V(x)}} \right)$$

$$\geqslant \frac{1}{\varphi_{+}} \left(\frac{\int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{x} dy \, e^{\beta V(y)}}{\int_{0}^{L} dx \, e^{-\beta V(x)}} - \frac{\int_{0}^{L} dx \, e^{-\beta V(x)} \int_{0}^{x} dy \, e^{\beta V(y)} \left(\int_{0}^{L} dz \, e^{\beta V(z)} \right)}{\left(\int_{0}^{L} dx \, e^{-\beta V(x)} \right)} \right) = 0.$$
(B20)

2. Strong tilt limit: $V'(x) \ll f$

Under this condition, V(x) is minor compared to the fx term. Thus, we expand $e^{\pm \beta V(x)}$ into a Taylor series,

$$I_{-}(x) = \int_{0}^{L} dy \, e^{-\beta[V(x) - V(x+y)]} e^{-\beta f y} = \int_{0}^{L} dy \left(1 + \beta V'(x) y + \frac{1}{2} \{ \beta^{2} [V'(x)]^{2} + \beta^{-1} V''(x) \} y^{2} + \cdots \right) e^{-\beta f y}$$

$$= \frac{1}{\beta f} \left(1 + \frac{V'(x)}{f} + \frac{\{ [V'(x)]^{2} + \beta^{-1} V''(x) \}}{f^{2}} + \cdots \right). \tag{B21}$$

Then

$$\langle I_{-}(x)\rangle_{L} = \frac{1}{\beta f} \left[1 + \frac{\langle [V'(x)]^{2}\rangle_{L}}{f^{2}} + \cdots \right], \tag{B22}$$

$$\langle I_{-}(x)\rangle_{L}^{3} = \frac{1}{\beta^{3} f^{3}} \left[1 + \frac{3\langle [V'(x)]^{2}\rangle_{L}}{f^{2}} + \cdots \right],$$
 (B23)

where $\langle V'(x)\rangle_L=0$ and $\langle V''(x)\rangle_L=0$ due to the periodicity of V(x) Next,

$$I_{-}^{2}(x)I_{+}(x) = I_{-}^{2}(x) \int_{0}^{L} dy \, e^{\beta[V(x) - V(x - y)]} e^{-\beta f y}$$

$$= I_{-}^{2}(x) \int_{0}^{L} dy \left(1 + \beta V'(x)y + \frac{1}{2} \{ \beta^{2} [V'(x)]^{2} + \beta^{-1} V''(x) \} y^{2} \cdots \right) e^{-\beta f y}$$

$$= I_{-}^{2}(x) \frac{1}{\beta f} \left(1 + \frac{V'(x)}{f} + \frac{[V'(x)]^{2} - \beta^{-1} V''(x)}{f^{2}} + \cdots \right), \tag{B24}$$

where $\lim_{\beta f L \gg 1} \frac{1}{(\beta f)^{n+1}} \int_0^{\beta f L} d\alpha \, \alpha^n e^{-\alpha} = \frac{n!}{(\beta f)^{n+1}}$ was used to evaluate the integrals in the second line. Then

$$\langle I_{-}^{2}(x)I_{+}(x)\rangle_{L} = \frac{1}{L} \int_{0}^{L} dx \frac{1}{\beta^{3} f^{3}} \left(1 + \frac{2V'(x)}{f} + \frac{3[V'(x)]^{2} + 2\beta^{-1}V''(x)}{f^{2}} + \cdots\right)$$

$$\times \left(1 + \frac{V'(x)}{f} + \frac{[V'(x)]^{2} - \beta^{-1}V''(x)}{f^{2}} + \cdots\right)$$

$$= \frac{1}{\beta^{3} f^{3}} \left(1 + \frac{3\sqrt{[V'(x)]^{2}}}{f} + \frac{6\sqrt{[V'(x)]^{2}}}{f^{2}} + \cdots\right)$$

$$= \frac{1}{\beta^{3} f^{3}} \left(1 + \frac{6\sqrt{[V'(x)]^{2}}}{f^{2}} + \cdots\right). \tag{B25}$$

Therefore, by taking the ratio between Eqs. (B25) and (B23), we get the following for $f \gg V'(x)$:

$$\frac{\langle [I_{-}(x)]^{2}I_{+}(x)\rangle_{L}}{\langle I_{+}(x)\rangle_{L}^{3}} = 1 + \frac{3\langle [V'(x)]^{2}\rangle_{L}}{f^{3}} + \dots \geqslant 1.$$
(B26)

Next, from the continuous version of Chebyshev's sum inequality, i.e., for real-valued, integrable functions X(x) and Y(x) satisfying $X'(x)Y'(x) \le 0$ for $\forall x \in [0,L]$, it holds that

$$\left(\frac{1}{L}\int_{0}^{L}X(x)dx\right)\left(\frac{1}{L}\int_{0}^{L}Y(x)dx\right) \geqslant \frac{1}{L}\int_{0}^{L}X(x)Y(x)dx. \tag{B27}$$

With the normalization condition $\int_0^L \rho_{ss}(x, f) dx = 1$, and setting $f(x) = \rho_{ss}(x, f)$ and $g(x) = \rho_{ss}^{-1}(x, f)$, it follows that

$$\frac{1}{L^2} \int_0^L \rho_{ss}^{-1}(x, f) dx \geqslant 1 \tag{B28}$$

for all f .

Thus, the following relation can be acquired for $f \gg V'(x)$:

$$Q(f)/2k_BT = \frac{1}{L^2} \int_0^L \rho_{ss}^{-1}(x, f) dx \times \frac{\langle [I_-(x)]^2 I_+(x) \rangle_L}{\langle I_+(x) \rangle_L^3} \geqslant 1 + \frac{3\langle [V'(x)]^2 \rangle_L}{f^3} + \dots \geqslant 1.$$
 (B29)

3. Near critical force $f \lesssim f_c$

Near critical force, $f \approx f_c$, the barriers of the potential vanish, and $\Phi(x, f)$ becomes almost flat over the period, (0, L). The shape of the potential would resemble a descending staircase with the period of L. In this case, we can approximate $\Phi(x + nL, f) = c - nfL$ for nL < x < (n + 1)L. Then,

$$\langle I_{+}(x)\rangle_{L} = \frac{1}{L} \int_{0}^{L} dx \, e^{\beta \Phi(x,f)} \int_{x-L}^{x} dy \, e^{-\beta \Phi(y,f)} \approx \frac{1}{L} \int_{0}^{L} dx \, e^{\beta c} \left(\int_{x-L}^{0} dy \, e^{-\beta(c+fL)} + \int_{0}^{x} dy \, e^{-\beta c} \right) = \frac{L}{2} (1 + e^{-\beta fL}) \quad (B30)$$

and

$$\langle [I_{+}(x)]^{2}I_{-}(x)\rangle_{L} = \frac{1}{L} \int_{0}^{L} dx \, e^{\beta\Phi(x,f)} \left(\int_{x-L}^{x} dy \, e^{-\beta\Phi(y,f)} \right)^{2} \left(\int_{x}^{x+L} dy \, e^{\beta\Phi(y,f)} \right)$$

$$\approx \frac{1}{L} \int_{0}^{L} dx \, e^{\beta c} \left(\int_{x-L}^{0} dy \, e^{-\beta(c+fL)} + \int_{0}^{x} dy \, e^{-\beta c} \right)^{2} \left(\int_{x}^{L} dy \, e^{\beta c} + \int_{L}^{L+x} dy \, e^{\beta(c-fL)} \right)$$

$$= \frac{L^{3}}{12} (1 + 5e^{-\beta fL} + 5e^{-2\beta fL} + e^{-3\beta fL}), \tag{B31}$$

which leads to

$$\frac{\langle [I_{+}(x)]^{2}I_{-}(x)\rangle_{L}}{\langle I_{+}(x)\rangle_{L}^{3}} = \frac{2}{3} \frac{(1 + 5e^{-\beta fL} + 5e^{-2\beta fL} + e^{-3\beta fL})}{(1 + e^{-\beta fL})^{3}}.$$
(B32)

Next.

$$\begin{split} \frac{1}{L^2} \int_0^L dx \, \rho_{\text{ss}}^{-1}(x, f) &\approx \frac{1}{L^2} \int_0^L dx \frac{e^{\beta c} (\psi_+(L, f) \psi_-(L, f) - f \Omega \int_0^L dx \, e^{-\beta c} \int_0^x dy \, e^{\beta c})}{\psi_+(L, f) - \Omega \int_0^x dy \, e^{\beta c}} \\ &= \frac{1}{L^2} \int_0^L dx \frac{e^{\beta c} (L^2 - \Omega L^2/2)}{e^{\beta c} L - \Omega e^{\beta c} x} = \int_0^L dx \frac{(1 - \Omega/2)}{L - \Omega x} = \frac{1 - \Omega/2}{\Omega} \log \frac{1}{1 - \Omega} = \frac{\beta f L}{2} \frac{1 + e^{-\beta f L}}{1 - e^{-\beta f L}}. \end{split} \tag{B33}$$

Therefore, from Eqs. (B32) and (B33) it follows that

$$\frac{\mathcal{Q}(f_c)}{2k_BT} = \frac{\beta f_c L}{3} \frac{(1 + 5e^{-\beta f_c L} + 5e^{-2\beta f_c L} + e^{-3\beta f_c L})}{(1 + e^{-\beta f_c L})^2 (1 - e^{-\beta f_c L})} \geqslant 1.$$
(B34)

Equation (B34) is a monotonically increasing function of $\beta f_c L$, greater than 1, and the equality sign is acquired when $\beta f_c L \rightarrow 0$.

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