

SupplementaryMaterial: Mesoscopic Non-equilibrium Thermodynamic Analysis of Molecular Motors

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Supplementary Material

0.1 Reaction rates

This part of the Supplementary Material gives the details of the section on Reaction rates in the main paper.

The flux along the reaction coordinates γ_1 and γ_2 can be described using Kramers theory (1, 2) and its activated nature can be used to identify the magnitude of J_{γ_1} and J_{γ_2} . The chemical potential of a molecular motor at temperature T , is given in terms of the motor enthalpy and the probability distributions $P_1(\gamma_1, t)$ or $P_2(\gamma_2, t)$ (where we have introduced the short-hand notation, $P_1(\gamma_1, t) \equiv P(x_a, \gamma_1, 0, t)$ and $P_2(\gamma_2, t) \equiv P(x_a, 1, \gamma_2, t)$) along the two reaction coordinates by

$$\mu_j(\gamma_j, t) = h_j(\gamma_j) + k_B T \ln [P_j(\gamma_j, t)] \quad (1)$$

where $h_j(\gamma_j)$ are the enthalpies (3) per molecular motor along the reaction paths, and where we have also introduced the short-hand notation, $\mu_{1(2)}(\gamma_1(\gamma_2), t) = \mu(x_a, \gamma_1(1), 0(\gamma_2), t)$ and $h_{1(2)}(\gamma_1(\gamma_2), t) = h(x_a, \gamma_1(1), 0(\gamma_2), t)$. A good approximation to $h_j(\gamma_j)$ may be derived from the potential of mean force of the motor in its activated or deactivated conformation. In equilibrium the chemical potential, μ_{eq} , is constant (independent of x, γ_1, γ_2, t). In this case we can then express

$$\mu_{eq} = k_B T \ln [P_{j,eq}(\gamma_j)] + h_j(\gamma_j) \quad (2)$$

which allows to write the motor equilibrium probability distribution as

$$P_{j,eq}(\gamma_j) = \exp \left[\frac{\mu_{eq} - h_j(\gamma_j)}{k_B T} \right]. \quad (3)$$

Along the first reaction path, the molecular motor goes from state d to state a and one ATP molecule is hydrolyzed to ADP and Pi. Therefore, $h_1(0) = h_d + h_{ATP} + h_{H_2O}$ and $h_1(1) = h_a + h_{ADP} + h_{Pi}$. Along the second reaction path the molecular motor goes from state a to state d. Using the same reference value we have $h_2(1) = h_d + h_{ADP} + h_{Pi}$ and $h_2(0) = h_1(1)$. When a fraction of the motors first moves from state d to a using the first reaction, and then from a to d using the second reaction, (both on the same position x_a), the reaction enthalpy $h_{ATP} - h_{ADP} - h_{Pi}$ is lost as heat in the surroundings. The enthalpy profiles associated to both reaction paths was illustrated in Figs. 3 and 4.

The reaction coordinates are characterized by high enthalpy barriers, larger than the thermal energy $k_B T$, at $\gamma_{1,0}$ and $\gamma_{2,0}$, which determine the corresponding transition states. As a consequence, the probability of finding molecular motors in the transition states is very small, both in equilibrium and away from equilibrium. Therefore, the enthalpies at the transition states can be referred to as the transition state energies, $h_1(\gamma_{1,0}) \equiv h_{1,0}$ and $h_2(\gamma_{2,0}) \equiv h_{2,0}$, see Figs. 3 and 4.

With large transition state energies, the reactions become slow and therefore quasi-stationary. In a quasi-stationary state, the reaction rates are independent of the reaction coordinate

$$J_{\gamma_j}(\gamma_j, t) = J_{\gamma_j}(t) [\theta(\gamma_j - 0) - \theta(\gamma_j - 1 - 0)] \quad (4)$$

where θ is the Heaviside function, which is zero for a negative and one for a positive argument ¹ The uniform value of the reaction flux implies that the chemical potential is roughly constant for reactants and products, at both sides of the transition state $\gamma_{j,0}$ (2)

$$\begin{aligned}\mu_1(\gamma_1, t) &= [\mu_d(t) + \mu_{\text{ATP}} + \mu_{\text{H}_2\text{O}}] \theta(\gamma_{1,0} - \gamma_1) + [\mu_a(t) + \mu_{\text{ADP}} + \mu_{\text{Pi}}] \theta(\gamma_1 - \gamma_{1,0}) \\ \mu_2(\gamma_2, t) &= [\mu_a(t) + \mu_{\text{ADP}} + \mu_{\text{Pi}}] \theta(\gamma_{2,0} - \gamma_2) + [\mu_d(t) + \mu_{\text{ADP}} + \mu_{\text{Pi}}] \theta(\gamma_2 - \gamma_{2,0})\end{aligned}\quad (5)$$

The first expression indicates that the molecular motor transition from state d to a couples uniquely to the reaction $\text{ATP} + \text{H}_2\text{O} \rightleftharpoons \text{ADP} + \text{Pi}$ of the fuel. We assume that the chemical potentials (concentrations) of ATP, H₂O, ADP and inorganic phosphate Pi are kept constant by buffering the system. In the second reaction $\mu_{\text{ADP}} + \mu_{\text{Pi}}$ only serves to indicate an activated state, comparable to a reference value. The uniform magnitude of the chemical potential at both sides of the transition state allows us to identify the chemical potential associated with the activated and deactivated states of the motor, $\mu_a(t)$ and $\mu_d(t)$ respectively. Quasi-stationarity leads to similar relations for other thermodynamic variables,

$$\begin{aligned}h_1(\gamma_1) &= [h_d + h_{\text{ATP}} + h_{\text{H}_2\text{O}}] \theta(\gamma_{1,0} - \gamma_1) + [h_a + h_{\text{ADP}} + h_{\text{Pi}}] \theta(\gamma_1 - \gamma_{1,0}) \\ h_2(\gamma_2) &= [h_a + h_{\text{ADP}} + h_{\text{Pi}}] \theta(\gamma_{2,0} - \gamma_2) + [h_d + h_{\text{ADP}} + h_{\text{Pi}}] \theta(\gamma_2 - \gamma_{2,0})\end{aligned}\quad (6)$$

for the enthalpy densities of the two chemical processes² and

$$\begin{aligned}P_1(\gamma_1, t) &= P_d(t) \theta(\gamma_{1,0} - \gamma_1) + P_a(t) \theta(\gamma_1 - \gamma_{1,0}) \\ P_2(\gamma_2, t) &= P_a(t) \theta(\gamma_{2,0} - \gamma_2) + P_d(t) \theta(\gamma_2 - \gamma_{2,0})\end{aligned}\quad (7)$$

for the corresponding probability distributions. Close to the transition states, for $\gamma_j \simeq \gamma_{j,0}$ all these variables change continuously from their values in the reactant and product basins: μ_j 's monotonously, h_j 's developing a large peak while P_j 's dip much below the constant values further away. The probability densities of a motor as it changes conformation are accessible; for example, in numerical studies they can be deduced from snapshots of the system's distribution of states.

It is well-known that the Onsager kinetic coefficients, $L_{\gamma_j}(\gamma_j, t)$, are usually in good approximation proportional to $P_j(\gamma_j, t)$. Accordingly, we introduce a diffusion coefficient for each reaction

$$D_{\gamma_j} \equiv k_B T \frac{L_{\gamma_j}(\gamma_j, t)}{P_j(\gamma_j, t)} \quad (8)$$

that can be regarded as constant. Due to the factor $k_B T$, D_{γ_j} have the dimensionality s^{-1} which is appropriate along the dimensionless reaction coordinates. Substituting the diffusion coefficients in the flux-force relations (11) in the main text. Using Eq.(15) from the main text, we obtain

$$J_{\gamma_j}(t) \exp \frac{h_j(\gamma_j)}{k_B T} = -D_{\gamma_j} \frac{\partial}{\partial \gamma_j} \exp \frac{\mu_j(\gamma_j, t)}{k_B T} \quad (9)$$

¹In order to ensure reactant and product conservation, the zero is in fact an infinitesimally small positive number and causes the reaction flux to be zero for $\gamma_j = 0$ and $\gamma_j = 1$, a property used to derive Eq.(6) in the main text.

²Taking h_i in good approximation constant away from $\gamma_{i,0}$ neglects factors $\exp[(h_i(x, t) - h(x, \gamma, t))/k_B T]$, for $i = 1, 2$, which allows one to derive simpler, explicit expressions for the quasi-steady reaction fluxes, as will be done in the next section.

which can be integrated over γ_j to get the magnitude of the quasi-steady reaction fluxes of the molecular motor,

$$\begin{aligned} J_{\gamma 1}(t) &= \frac{D_{\gamma 1}}{\int \exp \frac{h_1(\gamma_1)}{k_B T} d\gamma_1} \left[\exp \frac{\mu_d(t) + \mu_{\text{ATP}} + \mu_{\text{H}_2\text{O}}}{k_B T} - \exp \frac{\mu_a(t) + \mu_{\text{ADP}} + \mu_{\text{Pi}}}{k_B T} \right] \\ J_{\gamma 2}(t) &= \frac{D_{\gamma 2}}{\int \exp \frac{h_2(\gamma_2)}{k_B T} d\gamma_2} \left[\exp \frac{\mu_a(t) + \mu_{\text{ADP}} + \mu_{\text{Pi}}}{k_B T} - \exp \frac{\mu_d(t) + \mu_{\text{ADP}} + \mu_{\text{Pi}}}{k_B T} \right] \end{aligned} \quad (10)$$

which can be expressed compactly as

$$\begin{aligned} J_{\gamma 1}(t) &= J_{\gamma 1,+}(t) \left[1 - \exp \frac{\Delta G - \Delta\mu(t)}{k_B T} \right] \\ J_{\gamma 2}(t) &= J_{\gamma 2,+}(t) \left[1 - \exp \frac{\Delta\mu(t)}{k_B T} \right] \end{aligned} \quad (11)$$

where the unidirectional forward reaction rates are given by

$$\begin{aligned} J_{\gamma 1,+}(t) &= D_{\gamma 1} \left[\int \exp \frac{h_1(\gamma_1) - \mu_d(t) - \mu_{\text{ATP}} - \mu_{\text{H}_2\text{O}}}{k_B T} d\gamma_1 \right]^{-1} \\ J_{\gamma 2,+}(t) &= D_{\gamma 2} \left[\int \exp \frac{h_2(\gamma_2) - \mu_a(t) - \mu_{\text{ADP}} - \mu_{\text{Pi}}}{k_B T} d\gamma_2 \right]^{-1} \end{aligned} \quad (12)$$

and

$$\Delta\mu(t) \equiv \mu_d(t) - \mu_a(t) \quad \text{and} \quad \Delta G \equiv \mu_{\text{ADP}} + \mu_{\text{Pi}} - \mu_{\text{ATP}} - \mu_{\text{H}_2\text{O}}. \quad (13)$$

$\Delta\mu(t)$ and ΔG have been chosen so that they are both negative when the reaction proceeds from reactants to products. The absolute value of both is generally much larger than the thermal energy; in the system considered, the motor usually displaces in the regime $\Delta\mu(t) - \Delta G \gg k_B T$. It is also possible to extract the backward rate, when information is available on equilibrium exchange rates. This implies that both forward reaction rates are much larger than the backward reaction rates, so that in good approximation

$$J_{\gamma j}(t) \simeq J_{\gamma j,+}(t) \quad (14)$$

When $|\Delta\mu(t)|$ and $|\Delta G|$ are small compared to the thermal energy $k_B T$, one can linearize Eq.(11) leading to

$$J_{\gamma 1}(x, t) = -J_{\gamma 1,+}(x, t) \frac{\Delta G - \Delta\mu(t)}{k_B T} \quad \text{and} \quad J_{\gamma 2}(x, t) = -J_{\gamma 2,+}(x, t) \frac{\Delta\mu(t)}{k_B T}, \quad (15)$$

expressions one obtains using classical non-equilibrium thermodynamics. For example, in this regime, reaction rate of Eq.(1a) of the main text, $J_{\gamma 1}$, is proportional to a linear combination of ΔG for the ATP hydrolysis and the chemical potential difference of the activation step. The large values of $\Delta\mu$ and ΔG imply that the fluxes become nonlinear in the driving forces. The expressions of these fluxes

can be simplified taking advantage of the large magnitude of the transition state enthalpies, $h_{j,0}$, to approximate

$$\int \exp\left[\frac{h_j(\gamma_j)}{k_B T}\right] d\gamma_j = \exp\left[\frac{h_{j,0}}{k_B T}\right] \int \exp\left[\frac{h_j(\gamma_j) - h_{j,0}}{k_B T}\right] d\gamma_j \equiv C_{j,0} \exp\left[\frac{h_{j,0}}{k_B T}\right] \quad (16)$$

where the $C_{j,0}$ are constants of the order one. These expressions allow us to rewrite the forward fluxes

$$\begin{aligned} J_{\gamma 1,+}(t) &= \frac{D_{\gamma 1}}{C_{1,0}} \exp\left[\frac{\mu_d(t) + \mu_{\text{ATP}} + \mu_{\text{H}_2\text{O}} - h_{1,0}}{k_B T}\right] \\ J_{\gamma 2,+}(t) &= \frac{D_{\gamma 2}}{C_{2,0}} \exp\left[\frac{\mu_a(t) + \mu_{\text{ADP}} + \mu_{\text{Pi}} - h_{2,0}}{k_B T}\right] \end{aligned} \quad (17)$$

as expected from the law of mass action. Once the fluxes have been identified, it is possible to quantify the slipping of the molecular motor, $1 - z$, related to the conformational changes it experiences without ATP hydrolysis. In the usual regime at which the motor operates, using Eq.(14) from the main text and (14) one obtains for z

$$z \simeq 1 - \frac{J_{\gamma 2,+}}{J_{\gamma 1,+}} = 1 - \frac{D_{\gamma 2}}{D_{\gamma 1}} \frac{C_{1,0}}{C_{2,0}} \exp\left[\frac{\Delta\mu(t) - \Delta G + h_{1,0} - h_{2,0}}{k_B T}\right] \quad (18)$$

Close to thermal equilibrium z reduces to

$$z \simeq 1 - \frac{D_{\gamma 2}}{D_{\gamma 1}} \frac{C_{1,0}}{C_{2,0}} \frac{\Delta\mu(t)}{\Delta G - \Delta\mu(t)} \exp\left[\frac{h_{1,0} - h_{2,0}}{k_B T}\right] \quad (19)$$

0.2 Enthalpy profiles

In this section we derive an explicit expression for the effective enthalpy profile h , used in the main text is the section on Molecular Motor Displacement.

We use a simple model in which h_a is constant while $h_d(x) = c + d(1 - x)$ is a linear function which drops from $c + d$ to c between x equal to 0 and 1. Furthermore we take the diffusion coefficient D constant. In that case the effective enthalpy is given by (4)

$$h(\gamma_3) - h(0) = \int_0^{\gamma_3} d\alpha \lambda(\alpha) \frac{\partial}{\partial y} h_d(y) \quad (20)$$

The first and the second reaction take place at positions $x_a + n$ where n is an integer. γ_3 is taken to be zero in $x_a - 1$ and 1 in x_a . This implies that $y = x_a - 1 + \alpha$ in the integrand while $x = x_a - 1 + \gamma_3$. The derivative of the enthalpy in the domain of integration is $\partial h_d(y)/\partial y = -d(1 - \delta(y))$, where $\delta(y)$ is a delta function. $\lambda(\gamma_3)$ can be regarded as the fraction of deactivated motors along the filament coordinate, γ_3 , which are the ones that contribute to the inhomogeneous enthalpy, h . As we explained in the footnote below Eq.(9) in the main text, λ is a linear function of the position, $\lambda(\gamma_3) = a + b\gamma_3$ in the description we have given. λ therefore increases from a in $\gamma_3 = 0$ or $x = x_a - 1$ to $a + b$ in $\gamma_3 = 1$

or $x = x_a$. Note that both h_d and λ are periodic along the ligament with a period 1. Substituting λ and the derivative of h_d into Eq.(20) gives upon integration

$$h(\gamma_3) - h(0) = d \left[a (\theta(x) - \gamma_3) + b \left((1 - x_a) \theta(x) - \frac{1}{2} \gamma_3^2 \right) \right] \quad (21)$$

where $\theta(x)$ is the Heaviside function, which is zero for a negative argument and 1 for a positive argument. It follows from this equation that

$$h(\gamma_3 = 1) - h(\gamma_3 = 0) = db \left(\frac{1}{2} - x_a \right) \quad (22)$$

This illustrates the very important fact that the effective enthalpy is no longer a periodic function. For positive values of d and b , which is the natural choice in our model, and $x_a > 1/2$ the effective enthalpy decreases from interval to interval. It would be easy to obtain the effective enthalpy profile for a more general choice of λ , given that h_a and $h_d(x)$ are not changed. As this does not add much to our model we will not further pursue this.

References

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