Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

A model of chemomechanical coupling of myosin-V molecular motors

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S1. Studies of dynamics of myosin-V with tight-chemomechanical coupling model

Here, we explain the experimental data of Mehta et al. [S1] on the force dependence of dwell time (see Fig. 4a) using the tight-chemomechanical coupling model. For simplicity of treatment, we consider the simplest tight-chemomechanical coupling model, where we neglect backward stepping. In the model, an ATPase activity is tightly coupled with a forward mechanical step and the force dependence of the dwell time results solely from the force dependence of the rate constants of ATPase activity. It is important to note that *neglecting backward stepping cannot explain the experimental results on stepping ratio* (see Fig. 3a). Since in the range of the force used in the experiments of Mehta et al. [S1] (see Fig. 4a) the number of backward stepping is much smaller than that of the forward stepping, for an approximation, the effect of including backward stepping on the dwell time in the range of the force used in the experiments of Mehta et al. [S1] can be neglected.

Since ATP hydrolysis and actin-stimulated Pi release are much faster than ADP release, for an approximation, the ATPase rate of myosin-V head is determined only by rate constants of ADP release and ATP binding. Moreover, since the time of the mechanical movement is much shorter than the inverse of the ATPase rates, for an approximation, the dwell time is determined solely by the ATPase rate.

At saturated ATP, the ATPase rate k corresponds to the ADP-release rate k_D. Thus, the dwell time can be calculated by

$$T_{\mathrm{d}} = \frac{1}{k_{\mathrm{D}}}. \qquad \text{(S1)}$$

We assume that ADP release is composed of two substeps, with one substep having rate constant k_1 and the other one having rate constant k_2. Moreover, we assume that rate constant k_1 is independent of force F and rate constant k_2 is dependent on F, with $k_2 = k_{20}\exp\left[-F\delta/\left(k_{\mathrm{B}}T\right)\right]$, where k_{20} is rate constant of k_2 under F = 0 and δ is the characteristic distance. Thus, we have

$$\frac{1}{k_{\mathrm{D}}} = \frac{1}{k_1} + \frac{1}{k_{20}\exp\left[-F\delta/\left(k_{\mathrm{B}}T\right)\right]}. \qquad \text{(S2)}$$

Using Eqs. (S1) and (S2) and by adjusting k_1 = 10.8 s^{-1}, k_{20} = 1600 s^{-1} and δ = 12 nm, we fit the single-molecule data of Mehta et al. [S1] on the dwell time versus force at saturated ATP (2 mM) (Fig. S1).

Then, we consider non-saturated ATP. We denote by k_{bT} the second-order rate constant of ATP binding and assume that k_{bT} is force independent. The ATPase rate, k, can be calculated by

$$\frac{1}{k} = \frac{1}{k_{\mathrm{bT}}[\mathrm{ATP}]} + \frac{1}{k_{\mathrm{D}}}. \qquad \text{(S3)}$$

The dwell time can be calculated by

$$T_{\mathrm{d}} = \frac{1}{k}. \qquad \text{(S4)}$$

Using Eqs. (S2) – (S4), with values of k_1 = 10.8 s^{-1}, k_{20} = 1600 s^{-1} and δ = 12 nm (see above) and by additionally adjusting k_{bT} = 0.7 $\mu\mathrm{M}^{-1}\mathrm{s}^{-1}$, we fit the single-molecule data of Mehta et al. [S1] on the dwell time versus force at 1 μM ATP (Fig. S1). From Fig. S1, it is seen that the theoretical data under large forces are deviated far away from the experimental data. Specifically, under F = 2.7 pN, the theoretical value at 1 μM ATP is about 2-fold larger than the experimental value. This can be explained as follows. Under low force (e.g., F = 0.4 pN), since $1/k_{\mathrm{bT}}[\mathrm{ATP}]$ at 1 μM ATP is much larger than $1/k_{\mathrm{D}}$, the dwell time at 1 μM ATP is nearly equal to $1/k_{\mathrm{bT}}[\mathrm{ATP}]$. Under F = 2.7 pN, the dwell time is equal to $1/k_{\mathrm{D}}$ at saturated ATP (2 mM). The experimental data showed that the dwell time under F = 2.7 pN and at 2 mM ATP is close to that under F = 0.4 pN and at 1 μM ATP, implying that $1/k_{\mathrm{bT}}[\mathrm{ATP}]$ is close to $1/k_{\mathrm{D}}$. Thus, under F = 2.7 pN, the dwell time at 1 μM ATP, which is nearly equal to $1/k_{\mathrm{bT}}[\mathrm{ATP}] + 1/k_{\mathrm{D}}$, is about 2-fold larger than

that at 2 mM ATP, which is equal to $1/k_D$. Consequently, the tight chemomechanical coupling model dictates that under any force the dwell time at low ATP is always larger than that at high ATP.

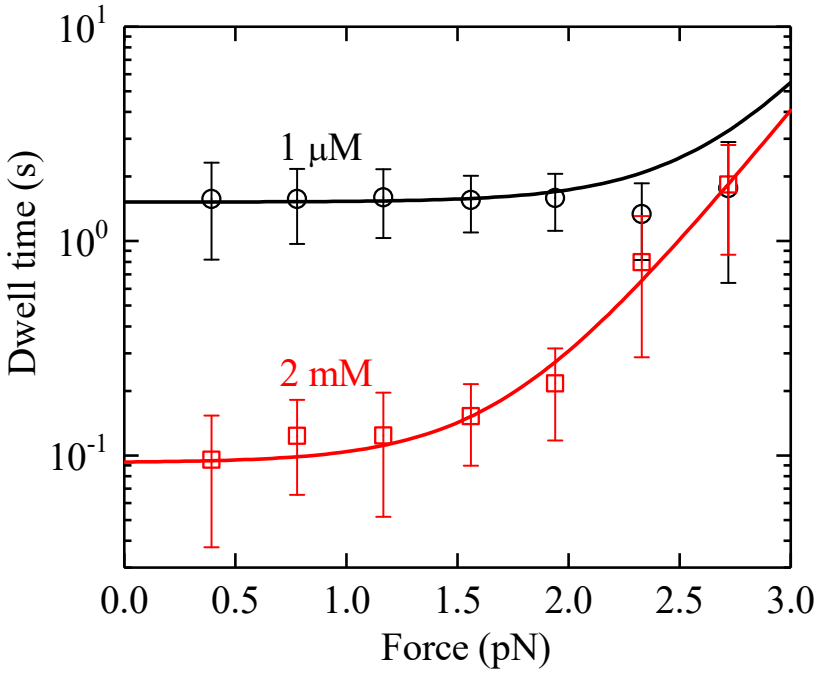

Fig. S1. Dwell time versus force at different ATP concentrations. Lines are theoretical data calculated using Eqs. (S1) – (S4) and with k_1 = 10.8 s^{-1}, k_{20} = 1600 s^{-1}, δ = 12 nm and k_{bT} = 0.7 $\mu M^{-1}s^{-1}$, and symbols are experimental data taken from Mehta et al. [S1].

References

[S1] Mehta A.D., Rock R.S., Rief M., Spudich J.A., Mooseker M.S., Cheney R.E. (1999) Myosin-V is a processive actin-based motor. Nature 400, 590–593.

S2. Dynamics of myosin-V with considering ATP-independent backward stepping

In the main text, we presented equations for the dynamics of myosin-V without considering the detachment of the head from actin in the strongly-binding state (ϕ or ADP state). Here, we present equations with considering the detachment of the head in the strongly-binding state. We only consider the detachment of the leading head in the strongly-binding state under the backward force *F*. The detachment rate in the strongly-binding state can be written as

$$\varepsilon = \varepsilon_0 \exp\left(F/F_d\right), \tag{S5}$$

where ε_0 is the detachment rate of the leading head in the strongly-binding state under $F = 0$ and F_d is the characteristic detachment force. Thus, during processive stepping, the rate constant of the leading head detaching from actin can be calculated by $k_\mathrm{D}^{(-)} + \varepsilon = k_\mathrm{D}^{(-)} + \varepsilon_0 \exp\left(F/F_d\right)$.

S2.1. At saturated ATP concnetration

As derived in the main text, probability P_E1 can be calculated by

$$P_\mathrm{E1} = \frac{\exp\left(\beta E_\mathrm{B}\right)\exp\left(-\alpha F\right)}{\exp\left(\beta E_\mathrm{B}\right)\exp\left(-\alpha F\right)+1}. \tag{S6}$$

Considering the detachment of the leading head in the strongly-binding state, the stepping ratio can be calculated by $r = P_\mathrm{E1} k_\mathrm{D}^{(+)} \Big/ \left\{\left(1-P_\mathrm{E1}\right)\left[k_\mathrm{D}^{(-)} + \varepsilon_0 \exp\left(F/F_d\right)\right]\right\}$. Substituting Eq. (S6) into above equation, we have

$$r = \frac{k_\mathrm{D}^{(+)}}{k_\mathrm{D}^{(-)}} \exp\left(\beta E_\mathrm{B}\right)\exp\left(-\alpha F\right) \frac{1}{1+\dfrac{\varepsilon_0 \exp\left(F/F_d\right)}{k_\mathrm{D}^{(-)}}}. \tag{S7}$$

With definitions $r_0 = \left(k_\mathrm{D}^{(+)}/k_\mathrm{D}^{(-)}\right)\exp\left(\beta E_\mathrm{B}\right)$ and $F_\mathrm{S} = \ln\left(r_0\right)/\alpha$ (see main text), Eq. (S7) can be rewritten as

$$r = r_0^{\left(1-F/F_\mathrm{S}\right)} \frac{1}{1+\dfrac{\varepsilon_0 \exp\left(F/F_d\right)}{k_\mathrm{D}^{(-)}}}. \tag{S8}$$

Similarly, with definitions $r_0 = \left(k_\mathrm{D}^{(+)}/k_\mathrm{D}^{(-)}\right)\exp\left(\beta E_\mathrm{B}\right)$ and $F_\mathrm{S} = \ln\left(r_0\right)/\alpha$, Eq. (S6) can be rewritten as

$$P_{\mathrm{E1}} = \frac{r_0^{(1-F/F_{\mathrm{S}})}}{r_0^{(1-F/F_{\mathrm{S}})} + \dfrac{k_{\mathrm{D}}^{(+)}}{k_{\mathrm{D}}^{(-)}}} . \tag{S9}$$

Eq. (S9) is identical to Eq. (4), as expected.

Considering the detachment of the leading head in the strongly-binding state, the velocity of the motor can be calculated by

$$v = \left\{ P_{\mathrm{E1}} k_{\mathrm{D}}^{(+)} - \left(1 - P_{\mathrm{E1}}\right)\left[k_{\mathrm{D}}^{(-)} + \varepsilon_0 \exp\left(F/F_d\right)\right]\right\} d . \tag{S10}$$

Substituting Eq. (S9) into Eq. (S10) we have

$$v = \frac{r_0^{(1-F/F_{\mathrm{S}})} - 1 - \dfrac{\varepsilon_0 \exp\left(F/F_{\mathrm{d}}\right)}{k_{\mathrm{D}}^{(-)}}}{r_0^{(1-F/F_{\mathrm{S}})} + \dfrac{k_{\mathrm{D}}^{(+)}}{k_{\mathrm{D}}^{(-)}}} k_{\mathrm{D}}^{(+)} d . \tag{S11}$$

Similarly, considering the detachment of the leading head in the strongly-binding state, the dwell time can be calculated by

$$T_{\mathrm{d}} = \frac{1}{P_{\mathrm{E1}} k_{\mathrm{D}}^{(+)} + \left(1 - P_{\mathrm{E1}}\right)\left[k_{\mathrm{D}}^{(-)} + \varepsilon_0 \exp\left(F/F_{\mathrm{d}}\right)\right]} . \tag{S12}$$

Substituting Eq. (S9) into Eq. (S12) we have

$$T_{\mathrm{d}} = \frac{r_0^{(1-F/F_{\mathrm{S}})} + \dfrac{k_{\mathrm{D}}^{(+)}}{k_{\mathrm{D}}^{(-)}}}{r_0^{(1-F/F_{\mathrm{S}})} + 1 + \dfrac{\varepsilon_0 \exp\left(F/F_{\mathrm{d}}\right)}{k_{\mathrm{D}}^{(-)}}} \frac{1}{k_{\mathrm{D}}^{(+)}} . \tag{S13}$$

Therefore, at saturated ATP, the stepping ratio, velocity and dwell time for myosin-V with considering ATP-independent backward stepping can be calculated by Eqs. (S8), (S11) and (S13), respectively. As expected, with ε_0 = 0, Eqs. (S8), (S11) and (S13) become Eqs. (2), (6) and (9), respectively. In Fig. S2 we show the force dependence of velocity and dwell time for different values of ε_0 and fixed F_{d} = 4.5 pN calculated using Eqs. (S11) and (S13) and with values of parameters r_0, F_{S}, $k_{\mathrm{D}}^{(+)}$ and $k_{\mathrm{D}}^{(-)}$ under the experimental condition of Uemura et al. [9] (see Table 1).

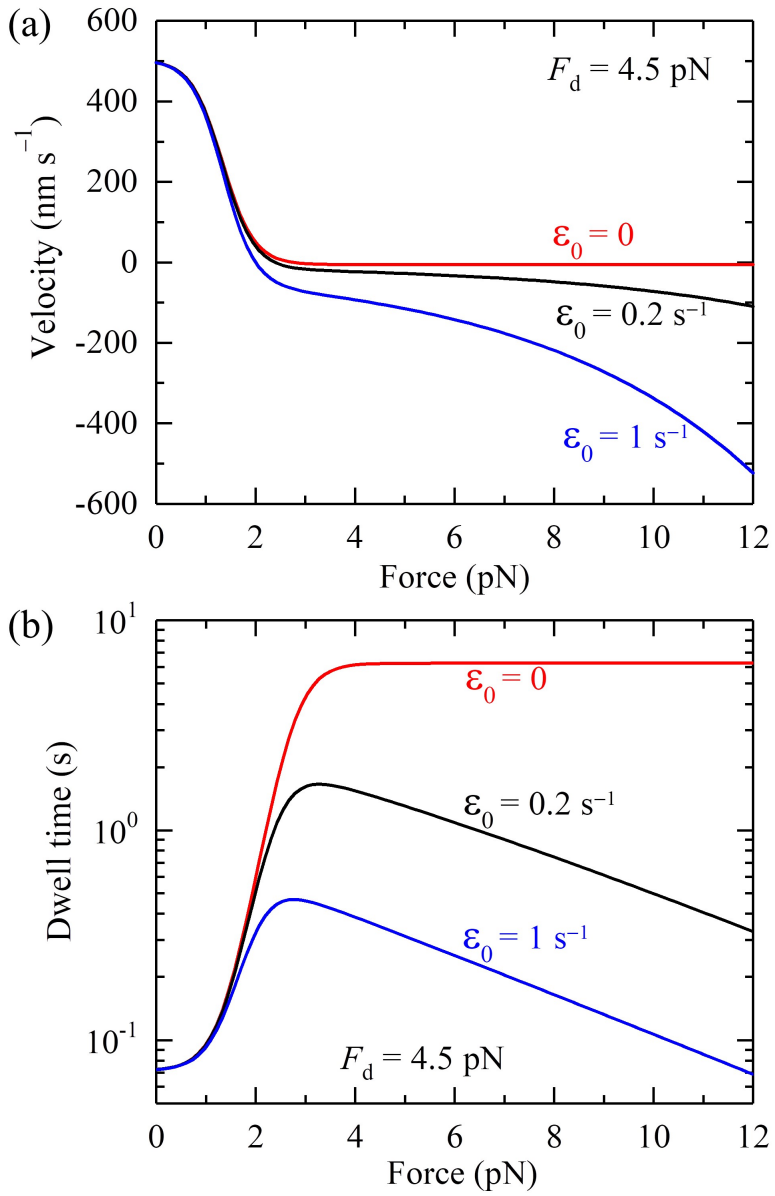

Fig. S2. Dynamics of myosin-V with inclusion of ATP-independent backward stepping. **(a)** Force dependence of velocity for different values of ε_0. **(b)** Force dependence of dwell time for different values of ε_0.

S2.2. At non-saturated ATP concentration

As given in the main text, we still have $P_{\mathrm{EF}} = P_{\mathrm{D}}^{(+)} P_{\mathrm{E1}} + \left(1 - P_{\mathrm{D}}^{(+)}\right) P_{\mathrm{E2}}$ and $P_{\mathrm{EB}} = P_{\mathrm{D}}^{(-)} \left(1 - P_{\mathrm{E1}}\right) + \left(1 - P_{\mathrm{D}}^{(-)}\right)\left(1 - P_{\mathrm{E2}}\right)$, where probabilities P_{E2}, $P_{\mathrm{D}}^{(+)}$ and $P_{\mathrm{D}}^{(-)}$ can still be calculated by Eqs. (11), (15) and (16), respectively.

Considering the detachment of the leading head in the strongly-binding state, the velocity of the motor can be calculated by $v=\left\{P_{\mathrm{EF}}k^{(+)}-P_{\mathrm{EB}}\left[k^{(-)}+\varepsilon_0\exp\left(F/F_d\right)\right]\right\}d$, where $k^{(+)}$ and $k^{(-)}$ can still be calculated by Eqs. (12) and (14), respectively. The above equation can be rewritten as

$$\frac{v}{d}=\left[P_{\mathrm{D}}^{(+)}P_{\mathrm{E1}}+\left(1-P_{\mathrm{D}}^{(+)}\right)P_{\mathrm{E2}}\right]k^{(+)}-\left[P_{\mathrm{D}}^{(-)}\left(1-P_{\mathrm{E1}}\right)+\left(1-P_{\mathrm{D}}^{(-)}\right)\left(1-P_{\mathrm{E2}}\right)\right]\left[k^{(-)}+\varepsilon_0\exp\left(F/F_d\right)\right]. \tag{S14}$$

Considering the detachment of the leading head in the strongly-binding state, the dwell time between two mechanical steps can be calculated by $T_{\mathrm{d}}=1\Big/\left\{P_{\mathrm{EF}}k^{(+)}+P_{\mathrm{EB}}\left[k^{(-)}+\varepsilon_0\exp\left(F/F_d\right)\right]\right\}$, which can be rewritten as

$$T_{\mathrm{d}}=\frac{1}{\left[P_{\mathrm{D}}^{(+)}P_{\mathrm{E1}}+\left(1-P_{\mathrm{D}}^{(+)}\right)P_{\mathrm{E2}}\right]k^{(+)}+\left[P_{\mathrm{D}}^{(-)}\left(1-P_{\mathrm{E1}}\right)+\left(1-P_{\mathrm{D}}^{(-)}\right)\left(1-P_{\mathrm{E2}}\right)\right]\left[k^{(-)}+\varepsilon_0\exp\left(F/F_d\right)\right]}. \tag{S15}$$