

## Supporting Information

**Derivation of the Smoluchowski equation for FB model :** According to the Liouville theorem ( $d\varphi/dt = 0$ ) the time evolution of probability density  $\varphi(x, r, t)$  in terms of  $x$  and  $r$  satisfies

$$\frac{\partial \varphi}{\partial t} = -\frac{\partial}{\partial x} \left( \frac{dx}{dt} \varphi \right) - \frac{\partial}{\partial r} \left( \frac{dr}{dt} \varphi \right). \quad (\text{S1})$$

Insertion of two Langevin equations (Eq.(1) in the main text) for the fluctuating bottleneck model  $\partial_t x = -\zeta^{-1}[\partial_x U_{\text{eff}}(x; r) + F_x(t)]$  and  $\partial_t r = -\lambda r + F_r(t)$  into Eq.S1 leads to

$$\begin{aligned} \frac{\partial \varphi}{\partial t} &= \frac{\partial}{\partial x} \left( \frac{1}{\zeta} \frac{dU_{\text{eff}}(x)}{dx} \varphi \right) + \frac{\partial}{\partial r} (\lambda r \varphi) - \frac{\partial}{\partial x} \left( \frac{1}{\zeta} F_x(t) \varphi \right) - \frac{\partial}{\partial r} (F_r(t) \varphi) \\ &\equiv -\mathcal{L}\varphi - \frac{\partial}{\partial \vec{a}} \cdot (\vec{F}(t)\varphi) \end{aligned} \quad (\text{S2})$$

where  $\vec{a} \equiv (x, r)$  and  $\vec{F}(t) \equiv (\frac{1}{\zeta} F_x(t), F_r(t))$ . Using the vector notation as in the second line of Eq.S2, one can formally solve for the probability density  $\varphi(\vec{a}, t)$  as

$$\varphi(\vec{a}, t) = e^{-t\mathcal{L}} \varphi(\vec{a}, 0) - \int_0^t ds e^{-(t-s)\mathcal{L}} \frac{\partial}{\partial \vec{a}} \cdot (\vec{F}(s)\varphi(\vec{a}, s)) \quad (\text{S3})$$

Averaging  $\varphi(\vec{a}, t)$  over noise after iterating  $\varphi(\vec{a}, t)$  into the noise related term in the integrand and exploiting the fluctuation-dissipation theorem, we obtain the Smoluchowski equation for  $\varphi(x, r, t)$  in the presence of a reaction sink,  $\mathcal{S}(x, r) = k_r r^2 \delta(x - x_{\text{ts}})$ ,

$$\frac{\partial \bar{\varphi}(x, r, t)}{\partial t} = [\mathcal{L}_x(x) + \mathcal{L}_r(r) - \mathcal{S}(x, r)] \bar{\varphi}(x, r, t), \quad (\text{S4})$$

where  $\mathcal{L}_x \equiv D\partial_x (\partial_x + (k_B T)^{-1} \partial_x U_{\text{eff}}(x))$  and  $\mathcal{L}_r \equiv \lambda\theta\partial_r (\partial_r + r/\theta)$ . Integrating both sides of the equation over  $x$  by defining  $\bar{C}(r, t) \equiv \int_{-\infty}^{\infty} dx \bar{\varphi}(x, r, t)$  leads to  $\partial_t \bar{C} = \mathcal{L}_r \bar{C}(r, t) - k_r r^2 \bar{\varphi}(x_{\text{ts}}, r, t)$ . By setting  $\bar{\varphi}(x_{\text{ts}}, r, t) = \phi_x(x_{\text{ts}}) \bar{C}(r, t)$  where  $\phi_x(x_{\text{ts}}) = e^{-U_{\text{eff}}(x_{\text{ts}})/k_B T} / \int dx e^{-U_{\text{eff}}(x)/k_B T} \approx$

$\sqrt{U''_{\text{eff}}(x_{\text{b}})/2\pi k_B T} e^{-(U_{\text{eff}}(x_{\text{ts}}) - U_{\text{eff}}(x_{\text{b}}))/k_B T}$ , we get

$$\partial_t \bar{C}(r, t) = [\lambda\theta\partial_r (\partial_r + r/\theta) - kr^2] \bar{C}(r, t), \quad (\text{S5})$$

where  $k \equiv k_r \sqrt{U''_{\text{eff}}(x_{\text{b}})/2\pi k_B T} e^{-\Delta U^\ddagger/k_B T}$  with  $\Delta U^\ddagger \equiv U(x_{\text{ts}}) - U(x_{\text{b}})$ . In all likelihood,  $k_r (= D \times \sqrt{U''_{\text{eff}}(x_{\text{ts}})/2\pi k_B T})$  represents the product of diffusion coefficient  $D$  associated with barrier crossing dynamics and the contribution of dynamics at the barrier top. Thus, under tension  $f$ , one can set  $k \rightarrow k(f) = k_0 e^{f\Delta x^\ddagger/k_B T}$  where  $k_0 \equiv (\xi D \sqrt{U''_{\text{eff}}(x_{\text{b}})U''_{\text{eff}}(x_{\text{ts}})/2\pi k_B T}) e^{-\Delta U^\ddagger/k_B T}$  and  $\xi$  describes the correction due to geometrical information of the cross section of bottleneck [1, 2]. Therefore, under tension  $f$ , Eq.S5 becomes Eq.(2) in the main text.

**Solution of the Smoluchowski equation with time-dependent sink :** For the problem with a constant loading rate, the sink function of our Smoluchowski equation becomes time-dependent, resulting in the following equation for the flux  $\bar{C}(r, t)$ ,

$$\frac{\partial \bar{C}(r, t)}{\partial t} = \lambda\theta \frac{\partial}{\partial r} \left( \frac{\partial}{\partial r} + \frac{r}{\theta} \right) \bar{C}(r, t) - k_0 r^2 e^{t(\gamma\Delta x^\ddagger/k_B T)} \bar{C}(r, t) \quad (\text{S6})$$

with  $\bar{C}(r, t=0) = \sqrt{\frac{2}{\pi\theta}} e^{-r^2/2\theta}$ . Although a time-dependent sink term, in general, makes Smoluchowski equations analytically intractable, the ansatz  $\bar{C}(r, t) \sim e^{\nu(t) - \mu(t)r^2}$  used in the Ref. [1] allows us to solve the above problem exactly. Substitution of  $\bar{C}(r, t) \sim e^{\nu(t) - \mu(t)r^2}$  leads to two ODEs for  $\nu(t)$  and  $\mu(t)$  (with ' denoting derivative

with respect to  $t$ ),

$$\nu'(t) = -2\lambda\theta\mu(t) + \lambda \quad (\text{S7})$$

and

$$\left(\mu(t) - \frac{1}{4\theta}\right)' = -4\lambda\theta\left(\mu(t) - \frac{1}{4\theta}\right)^2 + \frac{\lambda}{4\theta}\left(1 + \frac{4k_0\theta}{\lambda}e^{t\tilde{\gamma}}\right) \quad (\text{S8})$$

with  $\mu(0) = 1/2\theta$ . The equation for  $\mu(t)$  in Eq.S13 is the Riccati equation,  $y' = q_0(t) + q_1(t)y + q_2(t)y^2$  with  $y(t) \equiv \mu(t) - 1/4\theta$ . In general, the Riccati equation can be reduced to a second order ODE. The variable is changed in two steps : (i)  $v(t) = q_2(t)y(t)$  leads to  $v' = v^2 + P(t)v + Q(t)$  where  $Q = q_0q_2 = -\lambda^2\left(1 + \frac{4k_0\theta}{\lambda}e^{t\tilde{\gamma}}\right)$  and  $P = q_1 + q_2'/q_2 = 0$ . (ii) Another substitution  $v(t) = -u'(t)/u(t)$  leads to  $u''(t) - P(t)u'(t) + Q(t)u(t) = 0$ , i.e.,

$$u''(t) - \lambda^2\left(1 + \frac{4k_0\theta}{\lambda}e^{t\tilde{\gamma}}\right)u(t) = 0. \quad (\text{S9})$$

Introducing the variable  $\rho = \frac{2\lambda}{\tilde{\gamma}}\sqrt{\frac{4k_0\theta}{\lambda}}e^{t\tilde{\gamma}/2} = \beta\kappa(t)$  with  $\beta \equiv \frac{2\lambda}{\tilde{\gamma}}$  and  $\kappa(t) \equiv \sqrt{\frac{4k_0\theta}{\lambda}}e^{t\tilde{\gamma}/2}$  one can modify the second-order ODE in Eq.S9 into a more familiar modified Bessel equation,

$$\rho^2 U_{\rho\rho} + \rho U_{\rho} - [\beta^2 + \rho^2] U = 0 \quad (\text{S10})$$

where  $u(t) = U(\rho)$ . The solution of the above ODE is the linear combination of  $I_{\pm\beta}(\rho)$  for non-integer  $\beta$ , and the linear combination of  $I_{\beta}(\rho)$  and  $K_{\beta}(\rho)$  when  $\beta$  is integer. Thus, the solution of Eq.S10 is

$$U(\rho) = \begin{cases} c_1 I_{\beta}(\rho) + c_2 I_{-\beta}(\rho) & \beta \neq n, \beta > 0 \\ c_1 I_{\beta}(\rho) + c_2 K_{\beta}(\rho) & \beta = n \text{ where } n = 0, 1, 2, \dots \end{cases} \quad (\text{S11})$$

For simplicity, we use the notation  $\mathcal{Q}_{\beta}(\rho)$  to represent either  $I_{-\beta}(\rho)$  or  $K_{\beta}(\rho)$ ,

$$\mathcal{Q}_{\beta}(\rho) = \begin{cases} I_{-\beta}(\rho) & \beta \neq n, \beta > 0 \\ K_{\beta}(\rho) & \beta = n \text{ where } n = 0, 1, 2, \dots \end{cases} \quad (\text{S12})$$

Thus one obtains  $\mu(t)$  using  $y(t) = -\frac{u'(t)}{q_2(t)u(t)}$ .

$$\mu(t) = \frac{1}{4\theta} + \frac{\kappa(t)}{4\theta} \left( \frac{I'_{\beta}(\rho) + c\mathcal{Q}'_{\beta}(\rho)}{I_{\beta}(\rho) + c\mathcal{Q}_{\beta}(\rho)} \right). \quad (\text{S13})$$

Note that  $I'_{\beta}(\rho) \equiv dI_{\beta}(\rho)/d\rho$ . The initial condition  $\mu(0) = 1/2\theta$  determines the constant  $c$  in Eq.S13

$$c = \frac{I'_{\beta}(\rho_0) - [\kappa(0)]^{-1}I_{\beta}(\rho_0)}{[\kappa(0)]^{-1}\mathcal{Q}_{\beta}(\rho_0) - \mathcal{Q}'_{\beta}(\rho_0)}. \quad (\text{S14})$$

where  $\rho_0 \equiv \beta\kappa(0)$ . Thus, one obtains

$$\frac{\mu(t)}{\mu(0)} = \frac{1}{2} \left[ 1 + \kappa(t) \frac{\mathcal{I}'(\rho)}{\mathcal{I}(\rho)} \right] \quad (\text{S15})$$

where  $\mathcal{I}(\rho) \equiv \left( I'_{\beta}(\rho_0)\mathcal{Q}_{\beta}(\rho) - \mathcal{Q}'_{\beta}(\rho_0)I_{\beta}(\rho) \right) - [\kappa(0)]^{-1} \{ I_{\beta}(\rho_0)\mathcal{Q}_{\beta}(\rho) - \mathcal{Q}_{\beta}(\rho_0)I_{\beta}(\rho) \}$ . Recall that  $\rho \equiv \beta\kappa(t)$  with  $\beta \equiv 2\lambda/\tilde{\gamma}$ ,  $\kappa(t) \equiv \sqrt{\frac{4k_0\theta}{\lambda}}e^{t\tilde{\gamma}/2}$ , and  $\rho_0 \equiv \rho(0)$ . Note that  $\kappa(0)(\mathcal{I}'(\rho_0)/\mathcal{I}(\rho_0)) = 1$  is satisfied. Integration of Eq.S7 with  $t$  using Eq.S15 and change of variable  $d\rho = \frac{\beta\tilde{\gamma}}{2}\kappa(t)dt = \lambda\kappa(t)dt$  results in the expression for  $\nu(t)$ :

$$\nu(t) = \frac{\lambda t}{2} - \frac{1}{2} \log \left( \frac{\mathcal{I}(\rho)}{\mathcal{I}(\rho_0)} \right). \quad (\text{S16})$$

With  $\mu(t)$  (Eq.S15) and  $\nu(t)$  (Eq.S16) in hand, we can solve

$$\bar{C}(r, t) = \sqrt{\frac{2}{\pi\theta}} \left[ \frac{\mathcal{I}(\rho)}{\mathcal{I}(\rho_0)} \right]^{-1/2} \exp \left[ \frac{\lambda t}{2} - \frac{r^2}{4\theta} \left\{ 1 + \kappa(t) \frac{\mathcal{I}'(\rho)}{\mathcal{I}(\rho)} \right\} \right], \quad (\text{S17})$$

from which the survival probability is obtained as

$$\Sigma_{\lambda}^{\gamma}(t) = \int_0^{\infty} dr \bar{C}(r, t) = \frac{1}{\sqrt{2\theta}} \frac{e^{\nu(t)}}{\sqrt{\mu(t)}} = \sqrt{2} e^{\frac{\lambda t}{2}} \left[ \frac{\mathcal{I}(\rho)}{\mathcal{I}(\rho_0)} \right]^{-1/2} \left[ 1 + \kappa(t) \frac{\mathcal{I}'(\rho)}{\mathcal{I}(\rho)} \right]^{-1/2}. \quad (\text{S18})$$

The  $\lambda$ -dependent unbinding time distribution  $P_\lambda(t)$  are obtained from the relation  $P_\lambda(t) = -d\Sigma_\lambda^\gamma(t)/dt$ ,

$$P_\lambda(t) = \frac{\lambda e^{\lambda t/2}}{\sqrt{2}} \left[ \kappa^2(t) \frac{\mathcal{I}''(\rho)}{\mathcal{I}(\rho)} + \frac{1}{\beta} \kappa(t) \frac{\mathcal{I}'(\rho)}{\mathcal{I}(\rho)} - 1 \right] \left[ \frac{\mathcal{I}(\rho)}{\mathcal{I}(\rho_0)} \right]^{-1/2} \left[ 1 + \kappa(t) \frac{\mathcal{I}'(\rho)}{\mathcal{I}(\rho)} \right]^{-3/2}. \quad (\text{S19})$$

Transformation to the unbinding force distribution  $P_\lambda(\tilde{f}) [= \tilde{\gamma}^{-1} P_\lambda(t)]$  is made through the relationship between dimensionless scaled-force ( $\tilde{f}$ ) and time  $t$ :  $\tilde{f} = \tilde{\gamma} t$  with  $\tilde{\gamma} = \gamma \Delta x^\ddagger / k_B T$ .

**Illustration using synthetic data :** Although  $P_\lambda(\tilde{f})$  in Eq.S19 is complicated, the familiar expression used in the Dynamic Force Spectroscopy (DFS) for  $P(f)$  is restored when  $\lambda \rightarrow \infty$  (see below). In order to obtain insight into the behavior of  $P_\lambda(\tilde{f})$  we generated several synthetic distributions for varying  $\lambda$  values and loading rates. We find that  $P_\lambda(\tilde{f})$  with varying  $\tilde{\gamma} (= \gamma \Delta x^\ddagger / k_B T)$  shows the standard pattern of force distribution in DFS (Fig.S1-A, B) [2, 3]. The

effect of varying  $\lambda$  on  $P_\lambda(\tilde{f})$  is shown in Fig.S1-C, D. It is of particular interest that if  $\tilde{\gamma} \gg k_0 \theta$  then the most probable forces  $f_\lambda^*$  from  $P_\lambda(\tilde{f})$  are insensitive to the variation in  $\lambda$  even though the shapes of  $P_{\lambda \rightarrow 0}(\tilde{f})$  and  $P_{\lambda \rightarrow \infty}(\tilde{f})$  are very different from each other (Fig.S1-C). However, when  $\tilde{\gamma} \sim k_0 \theta$ ,  $f_\lambda^*$  changes with  $\lambda$  (Fig.S1-E) and the shape of  $P_{\lambda \rightarrow 0}(\tilde{f})$  differs from  $P_{\lambda \rightarrow \infty}(\tilde{f})$  qualitatively (Fig.S1-D).

**Asymptotic behavior at  $\lambda/\tilde{\gamma} \rightarrow \infty$  :** To obtain the asymptotic behavior we will use the following uniform asymptotic expansion of the modified Bessel function for large orders ( $\nu \rightarrow \infty$ ) [4].

$$\begin{aligned} I_\nu(\nu z) &\sim \frac{1}{\sqrt{2\pi\nu}} \frac{e^{\nu\eta}}{(1+z^2)^{1/4}} (1 + \mathcal{O}(\nu^{-1})) \\ K_\nu(\nu z) &\sim \sqrt{\frac{\pi}{2\nu}} \frac{e^{-\nu\eta}}{(1+z^2)^{1/4}} (1 + \mathcal{O}(\nu^{-1})) \\ I'_\nu(\nu z) &\sim \frac{1}{\sqrt{2\pi\nu}} \frac{(1+z^2)^{1/4}}{z} e^{\nu\eta} (1 + \mathcal{O}(\nu^{-1})) \\ K'_\nu(\nu z) &\sim -\sqrt{\frac{\pi}{2\nu}} \frac{(1+z^2)^{1/4}}{z} e^{-\nu\eta} (1 + \mathcal{O}(\nu^{-1})) \end{aligned} \quad (\text{S20})$$

where  $I'_\nu(\nu z) \equiv \frac{d}{d(\nu z)} I_\nu(\nu z)$  and  $\eta = \sqrt{1+z^2} + \log\left(\frac{z}{1+\sqrt{1+z^2}}\right)$

The asymptotic behavior at large negative orders can be obtained by using the relation  $I_{-\nu}(z) = \frac{2}{\pi} \sin(\nu\pi) K_\nu(z) + I_\nu(z)$

$$\begin{aligned} I_{-\nu}(\nu z) &\sim \left( \frac{2}{\sqrt{2\pi\nu}} \sin(\nu\pi) \frac{e^{-\nu\eta}}{(1+z^2)^{1/4}} + \frac{1}{\sqrt{2\pi\nu}} \frac{e^{\nu\eta}}{(1+z^2)^{1/4}} \right) (1 + \mathcal{O}(\nu^{-1})) \\ I'_{-\nu}(\nu z) &\sim \left( -\frac{2}{\sqrt{2\pi\nu}} \sin(\nu\pi) \frac{(1+z^2)^{1/4}}{z} e^{-\nu\eta} + \frac{1}{\sqrt{2\pi\nu}} \frac{(1+z^2)^{1/4}}{z} e^{\nu\eta} \right) (1 + \mathcal{O}(\nu^{-1})) \end{aligned} \quad (\text{S21})$$

Using these asymptotics, we obtain the following relations at  $\beta = 2\lambda/\tilde{\gamma} \rightarrow \infty$ .

$$\begin{aligned} \lim_{\beta \rightarrow \infty} \mathcal{I}(\rho) &\sim 2 \left( \frac{\sin \beta\pi}{\beta\pi} \right) \frac{1}{\kappa(0)} \left[ e^{\beta(\eta-\eta_0)} \left( 1 + \frac{1}{S(t)} \right) + e^{-\beta(\eta-\eta_0)} \left( 1 - \frac{1}{S(t)} \right) \right] \\ \lim_{\beta \rightarrow \infty} \mathcal{I}'(\rho) &\sim 2 \left( \frac{\sin \beta\pi}{\beta\pi} \right) \frac{1}{\kappa(0)\kappa(t)} \left[ e^{\beta(\eta-\eta_0)} (S(t) + 1) - e^{-\beta(\eta-\eta_0)} (S(t) - 1) \right] \end{aligned} \quad (\text{S22})$$

where  $S(t) \equiv (1 + \kappa^2(t))^{1/2}$ . Therefore

$$\lim_{\beta \rightarrow \infty} \frac{\mathcal{I}'(\rho)}{\mathcal{I}(\rho)} = \frac{S(t)}{\kappa(t)} \left[ \frac{(S(t) + 1) - (S(t) - 1)e^{-2\beta(\eta-\eta_0)}}{(S(t) + 1) + (S(t) - 1)e^{-2\beta(\eta-\eta_0)}} \right] \quad (\text{S23})$$

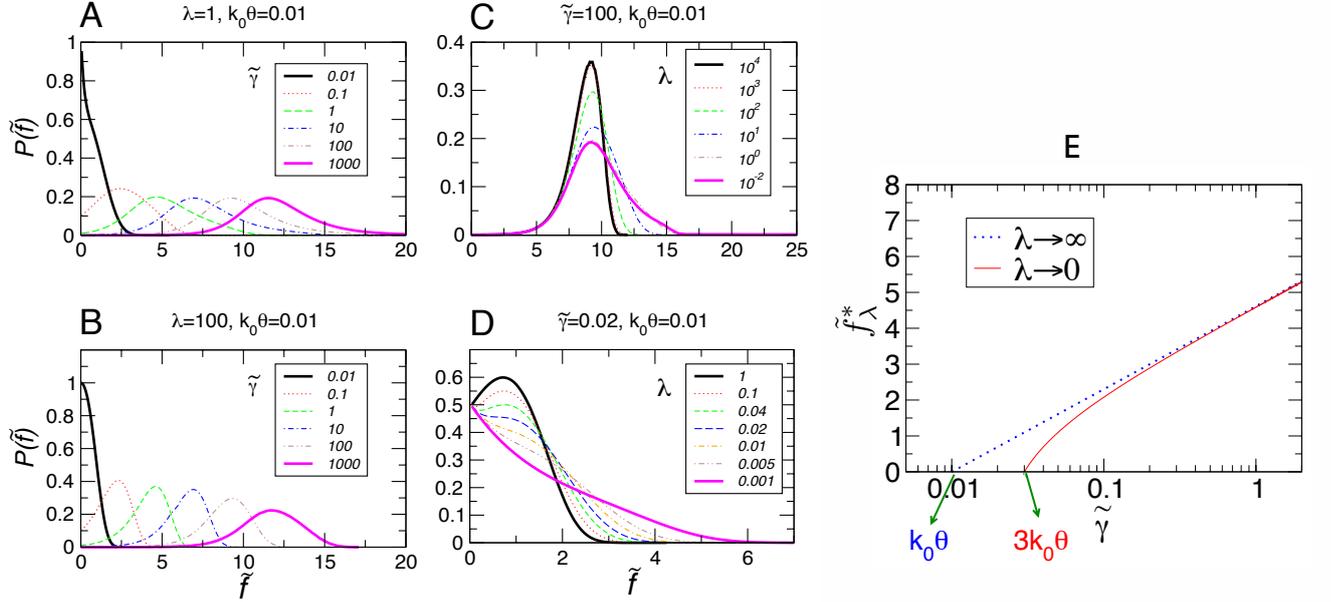


FIG. S1: **A-D** Rupture force distributions,  $P(\tilde{f})$ , under varying loading rates ( $\tilde{\gamma}$ ) and the gating frequency ( $\lambda$ ) characterizing the disorder. **E.**  $\tilde{f}^*$  vs  $\tilde{\gamma}$  plot under two limiting values of  $\lambda$ .

and

$$\lim_{\beta \rightarrow \infty} \frac{\mathcal{I}(\rho)}{\mathcal{I}(\rho_0)} = e^{\beta(\eta - \eta_0)} \left[ \frac{(S(t) + 1) - (S(t) - 1)e^{-2\beta(\eta - \eta_0)}}{2S(t)} \right]. \quad (\text{S24})$$

With  $\lim_{\tilde{\gamma} \rightarrow 0} S(t) = S$  and  $\lim_{\tilde{\gamma} \rightarrow 0} \beta(\eta - \eta_0) = \lambda St$  where  $S \equiv (1 + \frac{4k_0\theta}{\lambda})^{1/2}$ , it is now easy to show

$$\lim_{\tilde{\gamma} \rightarrow 0} \frac{\mu(t)}{\mu(0)} = \frac{1}{2} \left[ 1 + S \frac{(S+1) - (S-1)e^{-2\lambda St}}{(S+1) + (S-1)e^{-2\lambda St}} \right] \quad (\text{S25})$$

and

$$\lim_{\tilde{\gamma} \rightarrow 0} \nu(t) = -\frac{\lambda t}{2}(S-1) + \log \left[ \frac{(S+1) - (S-1)e^{-2\lambda St}}{2S} \right]^{-1/2}. \quad (\text{S26})$$

Thus, substituting Eq.S25 and S26 into  $\Sigma(t) = \int_0^\infty dr \bar{C}(r, t) = \frac{1}{\sqrt{2\theta}} \frac{e^{\nu(t)}}{\sqrt{\mu(t)}}$  recovers the previous result for survival probability in Zwanzig's FB model [1]

$$\lim_{\tilde{\gamma} \rightarrow 0} \Sigma(t) = \exp \left( -\frac{\lambda}{2}(S-1)t \right) \left[ \frac{(S+1)^2 - (S-1)^2 E}{4S} \right]^{-1/2}. \quad (\text{S27})$$

For  $\lambda \rightarrow \infty$  and  $\lambda \rightarrow 0$ ,  $\lim_{\lambda \rightarrow \infty} \lim_{\tilde{\gamma} \rightarrow 0} \Sigma(t) = \exp(-k\theta t)$  and  $\lim_{\lambda \rightarrow 0} \lim_{\tilde{\gamma} \rightarrow 0} \Sigma(t) = (1 + 2k\theta t)^{-1/2}$ , respectively.

**Survival probability ( $\Sigma(\tilde{f})$ ) and rupture force distribution ( $P(\tilde{f})$ ) for  $\lambda \rightarrow \infty$  and  $\lambda \rightarrow 0$  :** For

$\lambda \rightarrow \infty$ , taking  $\int_0^\infty dr(\dots)$  on Eq.S6 with pre-averaged rate constant  $k(t)\theta$  and transforming  $t$  into  $\tilde{f}$ , we obtain  $\tilde{\gamma} \partial_{\tilde{f}} \Sigma_{\lambda \rightarrow \infty}(\tilde{f}) = -k(\tilde{f})\theta \Sigma_{\lambda \rightarrow \infty}(\tilde{f})$ , which leads to

$$\Sigma_{\lambda \rightarrow \infty}(\tilde{f}) = \exp \left[ -\frac{1}{\tilde{\gamma}} \int_0^{\tilde{f}} d\tilde{f} k(\tilde{f})\theta \right] \quad (\text{S28})$$

and the rupture force distribution ( $P(\tilde{f}) = -d\Sigma(\tilde{f})/d\tilde{f}$ )

$$P_{\lambda \rightarrow \infty}(\tilde{f}) = \frac{1}{\tilde{\gamma}} k(\tilde{f}) \theta \Sigma_{\lambda \rightarrow \infty}(\tilde{f}) \quad (\text{S29})$$

The most probable force ( $\tilde{f}^*$ ) is obtained using  $[\partial_{\tilde{f}} P_{\lambda \rightarrow \infty}]_{\tilde{f}=\tilde{f}^*} = 0$ , which is equivalent to  $\tilde{\gamma}[\partial_{\tilde{f}} k(\tilde{f})]_{\tilde{f}=\tilde{f}^*} = [k(\tilde{f})]_{\tilde{f}=\tilde{f}^*}^2 \theta$ . Using  $k(\tilde{f}) = k_0 e^{\tilde{f}}$ , one can easily show that

$$\tilde{f}_{\lambda \rightarrow \infty}^* = \log[\tilde{\gamma}/(k_0 \theta)]. \quad (\text{S30})$$

This expression is equivalent to the standard DFS theory except for the presence of the  $\theta$  term. The fast variation of  $r$ -coordinate effectively modifies the reactivity  $k_0 r^2$  into  $k_0 \theta$ .

For  $\lambda \rightarrow 0$  the bottleneck radius is quenched to a single value, say,  $r_0$ . In this case the noise-averaged probability of the molecule found at the configuration of  $r_0$  at force  $\tilde{f}$ ,  $\bar{C}(r_0, \tilde{f}) = \exp\left(-\frac{1}{\tilde{\gamma}} \int_0^{\tilde{f}} d\tilde{f} k(\tilde{f}) r_0^2\right)$ , should be weighted by  $\phi(r_0) \left[= \sqrt{\frac{2}{\pi\theta}} e^{-r_0^2/2\theta}\right]$  as  $\Sigma_{\lambda \rightarrow 0}(\tilde{f}) = \int_0^\infty dr_0 \bar{C}(r_0, \tilde{f}) \phi(r_0)$  to give the survival probability,

$$\Sigma_{\lambda \rightarrow 0}(\tilde{f}) = \left[1 + \frac{2\theta}{\tilde{\gamma}} \int_0^{\tilde{f}} d\tilde{f} k(\tilde{f})\right]^{-1/2}. \quad (\text{S31})$$

A similar procedure as in Eqs. S29 and S30 leads to

$$P_{\lambda \rightarrow 0}(\tilde{f}) = \frac{1}{\tilde{\gamma}} k(\tilde{f}) \theta \left[\Sigma_{\lambda \rightarrow 0}(\tilde{f})\right]^3 \quad (\text{S32})$$

and

$$\tilde{f}_{\lambda \rightarrow 0}^* = \log\{(\tilde{\gamma}/k_0 \theta)(1 - 2k_0 \theta/\tilde{\gamma})\}. \quad (\text{S33})$$

**Comparison between  $P_{\lambda \rightarrow \infty}(\tilde{f})$  and  $P_{\lambda \rightarrow 0}(\tilde{f})$  one-dimensional models :** Asymptotic behaviors of  $P(f)$  with two limiting  $\lambda$  values at large  $\tilde{f} \gg \tilde{f}^*$ ,  $P_{\lambda \rightarrow \infty}(\tilde{f})$  and  $P_{\lambda \rightarrow 0}(\tilde{f})$  are obtained by using the Bell model for  $k(\tilde{f})$ . Comparison between  $P_{\lambda \rightarrow \infty}(\tilde{f})$  and  $P_{\lambda \rightarrow 0}(\tilde{f})$  can be made by using the explicit form of  $k(\tilde{f}) = k_0 e^{\tilde{f}}$ .

$$P_{\lambda \rightarrow \infty}(\tilde{f}) = \frac{k_0 \theta}{\tilde{\gamma}} \exp\left[\tilde{f} - \frac{k_0 \theta}{\tilde{\gamma}} (e^{\tilde{f}} - 1)\right] \quad (\text{S34})$$

and

$$P_{\lambda \rightarrow 0}(\tilde{f}) = \frac{k_0 \theta}{\tilde{\gamma}} \exp(\tilde{f}) \left[1 + 2\frac{k_0 \theta}{\tilde{\gamma}} (e^{\tilde{f}} - 1)\right]^{-3/2}. \quad (\text{S35})$$

For  $\tilde{f} \rightarrow \infty$ ,  $P(\tilde{f})$  behaves as

$$\begin{aligned} \lim_{\tilde{f} \rightarrow \infty} \log P_{\lambda \rightarrow \infty}(\tilde{f}) &\sim \tilde{f} - \frac{k_0 \theta}{\tilde{\gamma}} \exp(\tilde{f}) \\ \lim_{\tilde{f} \rightarrow \infty} \log P_{\lambda \rightarrow 0}(\tilde{f}) &\sim -\tilde{f}/2. \end{aligned} \quad (\text{S36})$$

It is worth noting that depending on the  $\lambda$  value ( $\lambda \rightarrow \infty$  or 0)  $P_{\lambda}(\tilde{f})$  differs in its asymptotic behavior with respect to  $f$  (see Eqs.S35 and S36).

The asymptotic behavior of the so-called microscopic model [5, 6], whose force range is limited by the critical force ( $f < f_c = \Delta G^\ddagger/\nu \Delta x^\ddagger$ ), is reduced to that of Gumbel distribution only if  $f^* < f \ll f_c$ . If  $f^* < f \rightarrow f_c$  then the unbinding force distribution decays precipitously to zero as  $\sim (1 - f/f_c)^{1/\nu-1}$  ( $\nu = 2/3$ : cubic potential) and linearly ( $\nu = 1/2$ : harmonic cusp potential) ( $\lambda \rightarrow \infty$  corresponds to the Bell model). Note that the model in [5, 6] corresponds to  $\lambda \rightarrow \infty$ .

In contrast, for  $\tilde{f} \rightarrow 0$ ,

$$\begin{aligned} \lim_{\tilde{f} \rightarrow 0} P_{\lambda \rightarrow \infty}(\tilde{f}) &\sim \frac{k_0 \theta}{\tilde{\gamma}} \times \exp\left[\left(1 - \frac{k_0 \theta}{\tilde{\gamma}}\right) \tilde{f}\right] \\ \lim_{\tilde{f} \rightarrow 0} P_{\lambda \rightarrow 0}(\tilde{f}) &\sim \frac{k_0 \theta}{\tilde{\gamma}} \times \left[1 + \left(1 - 3\frac{k_0 \theta}{\tilde{\gamma}}\right) \tilde{f} + \mathcal{O}(\tilde{f}^2)\right]. \end{aligned} \quad (\text{S37})$$

The initial slope of  $P(\tilde{f})$  is determined by the value of  $k_0 \theta/\tilde{\gamma}$ .

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