SUPPORTING INFORMATION

On detection of single bond ruptures in force spectroscopy by AFM

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S1. Analytical models of survival probability in dynamic force spectroscopy

Analytical expressions for the survival probability are most often derived for constant loading rate, that is when the loading force increases linearly with time: $F = v_F \cdot t$. In this case, the survival probability can be obtained for forced dissociation of molecules are held together by a potential that can have different shapes: triangular potential, parabolic potential with cusp barrier, cubic-linear potential, and approximate Morse potential.[1-7] For example, when the loading rate is constant and the dissociation rate increases exponentially with force according to the Bell model[8] $k(F) = k_0 \exp(F\, x^{\ddagger}/(k_B T))$ then the survival probability is given by

$$s(F) = \exp\left(-k_0 F^{\ddagger}\left(\exp\left(\frac{F}{F^{\ddagger}}\right) - 1\right)/v_F\right) \tag{S1}$$

Here $x^{\ddagger}$ is the distance along the pulling coordinate from the equilibrium position to the transition state, k_B is the Boltzmann constant, T is the temperature, $F^{\ddagger} = k_B T / x^{\ddagger}$, $v_F = dF/dt$ is the loading rate and k_0 is the dissociation rate at zero force.

When a molecular bond is loaded via polymeric tethers, the loading rate is not constant. The FJC model is often used to describe the stretching of polymeric tethers.[9-12]

$$x = L_c\left(\coth\left(\frac{F}{F_K}\right) - \frac{F_K}{F}\right) \tag{S2}$$

where x is the mean separation between tether ends and L_c is the contour length of the tether, b is the Kuhn length and $F_K = k_B T / b$.. The analytical expression for the survival probability using the high-force asymptotic behavior of FJC (aFJC) tethers ($F = F_K/(1 - x/L_c)$) is reasonably accurate for pulling forces exceeding ~$3F_K$.[9] The survival probability in this case can be calculated by replacing the lower integration limit in eq. 8 with F_K. The result is given by

$$s(F) = \exp\left[-\frac{k_0}{F^{\ddagger} F v_F^0}\left(F_c F_K F\left(\mathrm{Ei}\left(\frac{F}{F^{\ddagger}}\right) - \mathrm{Ei}\left(\frac{F_K}{F^{\ddagger}}\right)\right) + F^{\ddagger}\left(F_c F e^{\frac{F_K}{F^{\ddagger}}} + e^{\frac{F}{F^{\ddagger}}}(F^{\ddagger}F - F_c F_K) - F^{\ddagger}F\right)\right)\right] \tag{S3}$$

Here, in addition to the notation described above, $F_c = L_c \cdot k_c$, $v_F^0 = k_c \cdot v$ is the "nominal" loading rate, v is velocity of the force sensor (e.g. cantilever in AFM experiments), k_c is the spring constant of the force sensor, and "Ei" is the exponential integral function defined as $\mathrm{Ei}(x) = -\int_{-x}^{\infty} \frac{e^{-t}}{t} dt$.

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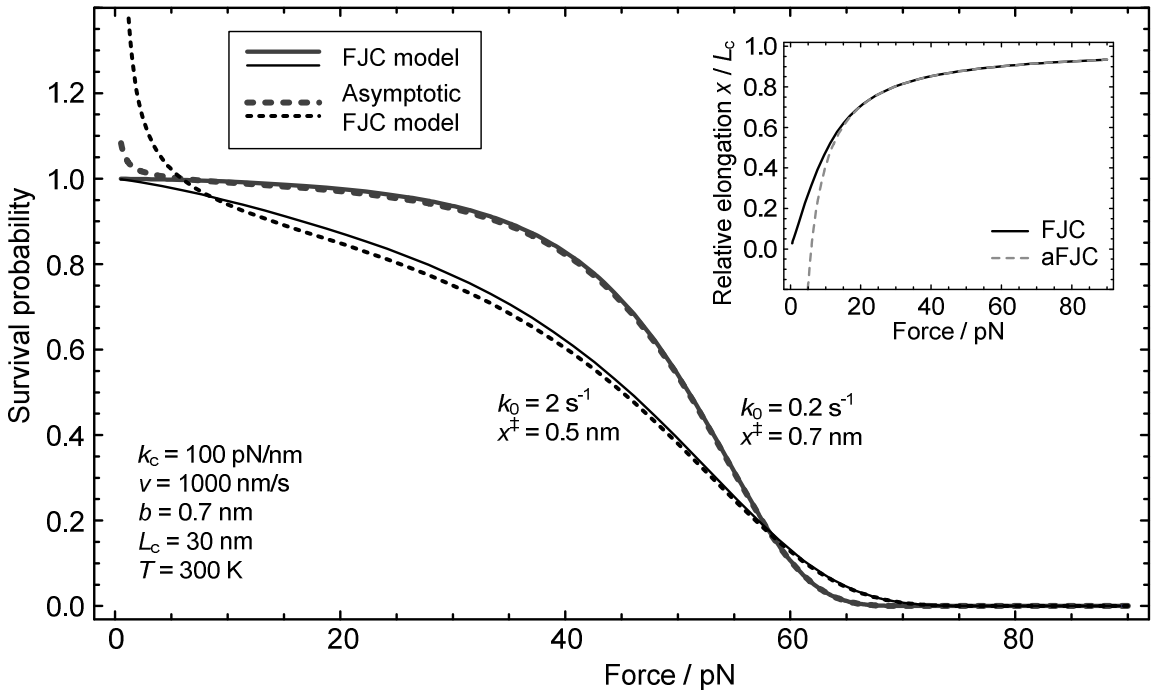

Figure S1. Comparison of survival probabilities calculated using the FJC and aFJC tether models by eq. S5 and eq S3, respectively. The legend is shown in the figure. The two sets of parameters used in the calculations are shown next to the corresponding curves. Other parameters are also indicated in the figure. Note that the asymptotic FJC model gives false survival probability values (>1) at low forces. The inset shows elongation vs. force dependence for the FJC and aFJC models.

However, when two tethers of significantly different length are pulled in parallel, the force on the longer tether might be outside of the range of the applicability of the aFJC model. Moreover, the survival probability calculated using the aFJC model shows a noticeable deviation from the accurate values for bonds with relatively short natural bond lifetime (k_0^{-1}), if these are pulled by long tethers. This is illustrated by two examples in Fig. S1. Here the deviation of the result given by the model (eq. S3) from the accurate results is noticeable for the bond lifetime of 0.5 s, while it takes approximately ten times shorter to stretch the polymer to apply a restoring force similar to the most probable rupture force. Therefore we have derived an analytical expression for the bond survival probability using Bell's model for the dissociation kinetics and the FJC model (eq. S2) to describe the dynamics of the loading. In this derivation, eq. 8 (main text) is integrated with the loading rate given by

$$v_F(F) = \frac{v_F^0 F^2 F_K}{F_K(F^2 + F_K F_c) - F^2 F_c \operatorname{csch}^2\left(\frac{F}{F_K}\right)} \qquad \text{(S4)}$$

Eq. S4 can also be used in the calculation of the pdf by eq. 9 in the main text. The resulting expression for the survival probability is

$$s(F) = \exp\left[-\frac{k_0}{F^{\ddagger} F v_{\mathrm{F}}^0 (2F^{\ddagger} - F_{\mathrm{K}})}\left(2F_{\mathrm{c}}F_{\mathrm{K}}F(2F^{\ddagger} - F_{\mathrm{K}})\mathrm{Ei}\left(\frac{F}{F^{\ddagger}}\right) + \right.\right.$$

$$(2F^{\ddagger} - F_{\mathrm{K}})[F\left(2\,F_{\mathrm{c}}F_{\mathrm{K}}\left(\log\left(\frac{2F^{\ddagger}}{F_{\mathrm{K}}}\right) + \pi\cot\left(\frac{\pi F_{\mathrm{K}}}{2F^{\ddagger}}\right) + \psi^{(0)}\left(\frac{F_{\mathrm{K}}}{2F^{\ddagger}}\right)\right) + 2\,F^{\ddagger}(F_{\mathrm{c}} - F^{\ddagger})\right) +$$

$$2F^{\ddagger}e^{\frac{F}{F^{\ddagger}}}\left(F\left(F^{\ddagger} + \coth\left(\frac{F}{F_{\mathrm{K}}}\right) - F_{\mathrm{c}}\ {}_2F_1\left(1, -\frac{F_{\mathrm{K}}}{2F^{\ddagger}}, 1 - \frac{F_{\mathrm{K}}}{2F^{\ddagger}}, e^{-\frac{2F}{F_{\mathrm{K}}}}\right)\right) - F_{\mathrm{c}}F_{\mathrm{K}}\right) \quad] +$$

$$\left.2F_{\mathrm{c}}F_{\mathrm{K}}F^{\ddagger}Fe^{F\left(\frac{1}{F^{\ddagger}} - \frac{2}{F_{\mathrm{K}}}\right)}\ {}_2F_1\left(1, 1 - \frac{F_{\mathrm{K}}}{2F^{\ddagger}}, 2 - \frac{F_{\mathrm{K}}}{2F^{\ddagger}}, e^{-\frac{2F}{F_{\mathrm{K}}}}\right)\right] \qquad \text{(S5)}$$

Here $\psi^{(0)}$ is the digamma function, and ${}_2F_1$ is the hypergeometric function.[13] Equation S5 is cumbersome and it uses several special functions; however these functions are available in contemporary mathematical packages and thus the equation is straightforward to use in data analysis. In calculations that employ eq. S5, we approximate the hypergeometric function using a series expansion.[13]

S2. Simultaneous two-bond ruptures using different models of dissociation kinetics and loading dynamics.

Here we show the results of the calculations comparing the Bell model with FJC loading and two kinetic models of forced dissociation: a model with escape from paraboloidal potential with a cusp barrier ("cusp" model in the legend below) and one with escape from the cubic-linear potential ("cubic" model in the legend below).[7] In addition, the loading dynamics is considered to occur according to the model of stretching a poly(ethylene glycol) (PEG) tether in water (PEG-FJC model).[14] To use these models, we perform numeric calculations as described earlier.[15-17] Using the model described in the main text, we have determined what fraction of the rupture measurements corresponds to the ruptures of single molecular bonds, for different ratios of the first and the second tether lengths. The results of calculations are shown in Fig. S2. The parameters indicated in the figure are: $x^{\ddagger}$ is the distance along the pulling coordinate from the equilibrium position to the transition state; k_0 is the dissociation rate at zero force; A is the Arrhenius pre-exponential factor; v is the probe velocity; k_c is the spring constant of the cantilever force sensor; L_c is the contour length of the first tether; b is the Kuhn length; and T is the temperature. It can be noticed from the graphs shown in Fig. S2, that the different models predict qualitatively similar results.

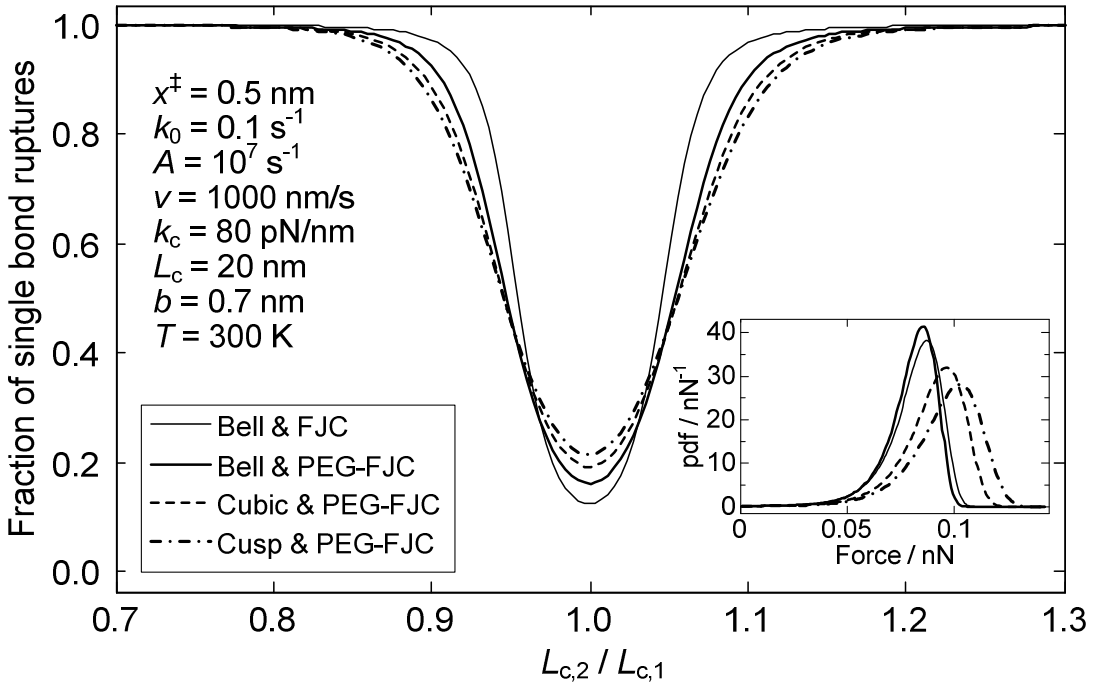

Figure S2. Fraction of the apparent single bond ruptures for different dissociation kinetics and loading dynamics models as indicated by the legend. The inset shows the corresponding pdf's of single bond ruptures. Parameters used in the calculations are shown in the figure.

S3. References

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