SUPPORTING INFORMATION : Refolding dynamics of stretched biopolymers upon force-quench

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T-quench versus f-quench dynamics : Our work also provides insights into the qualitative differences between the two-state dynamics upon force or temperature variations (compare $P_{TDE}(R)$ and $P_S(R)$ in Fig.2). For an apparent two-state folder, the fraction of folded states is $\varphi_{NBA}(f) = 1/[1+e^{-(\Delta F^o_{UF} - f\Delta x_{UF})/k_BT}]$. The half-width of fluctuations ($\delta f_{1/2}$) around transition mid-force $f_m = \Delta F_{UF}/\Delta x_{UF}$ using $d\varphi_{NBA}(f)/df$ is

$$\delta f_{1/2} = \frac{k_BT}{\Delta x_{UF}} \log \sqrt{\frac{3+2\sqrt{2}}{3-2\sqrt{2}}} \approx 1.7 \times \frac{k_BT}{\Delta x_{UF}}. \tag{1}$$

$\Delta x_{UF} \approx 6$ nm for P5GA hairpin [1] (see Fig.S3), thus $\delta f_{1/2} \approx 1.2$ pN at $k_BT = 4.14\ pN \cdot nm$. For the folded state to be predominantly populated after the force is quenched, the depth of quench should satisfy $\delta f_Q = f_m - f_Q > \delta f_{1/2} \approx 1.2$ pN. It is noteworthy that only the characteristic force $k_BT/\Delta x_{UF}$ determines the sharpness of the transition ($\delta f_{1/2}$), while ΔF_{UF} plays no significant role. Since $\Delta x_{UF} \sim N$, it follows that $\delta f_{1/2} \sim 1/N$, which differs from the thermodynamic scaling upon temperature variation, $(T_\Theta - T)/T_\Theta = \delta T/T_\Theta \sim 1/\sqrt{N}$ [2, 3]. Thus, for a given length N, the force-induced transition is sharper than the temperature-induced transition [4]. Since $\exp(f_Q \Delta x^\ddagger_{U\to N}/k_BT) = \exp(f_m \Delta x^\ddagger_{U\to N}/k_BT)\exp(-\delta f_Q \Delta x^\ddagger_{U\to N}/k_BT)$, a larger depth of quench exponentially increase the rate of folding by lowering the free energy barrier associated with refolding dynamics from the UBA, in contrast to the homopolymer following a temperature quench ($\tau_c \approx \tau_R \delta T/T_\Theta$) [3].

Calculation of P_{RSE} and P_{TSE}: To calculate $P_{RSE}(R)$ over the time traces, we collect the data points from $50 < t < 70$ μs for $f_S = 56$ pN, and $10 < t < 30$ μs for $f_S = 14$ pN. Similarily, to calculate $P_{TSE}(R)$ over the time traces, the data are collected from $\tau_F(i) - 270 < t < \tau_F(i) - 250$ μs for all f_Q values, where $\tau_F(i)$ denotes the folding time of i^{th} trajectory.

Dependence of folding time of P5GA hairpins on stretch- (f_S) and quench-forces (f_Q) : For a given survival probability ($\Sigma(t) = R(t; f_S, f_Q)/R(0; f_S)$) the average folding time is obtained by using $\tau_F(f_S, f_Q) = \int_0^\infty dt \Sigma(t; f_S, f_Q)$. The force f_S determines the initial distribution of molecules in the UBA and NBA, and is giving the Boltzmann distribution. To probe folding we are interested in the dynamics of molecules that are initially in the UBA. The fraction of molecules in the UBA for the two state RNA hairpin is $\varphi_{UBA}(f_S) =$

$\left(1+e^{(\Delta F_{UN}-f_S\Delta x_{UN})/k_BT}\right)^{-1}=\left(1+e^{(-\delta f_S\Delta x_{UN})/k_BT}\right)^{-1}$ where $f_S=f_m+(f_S-f_m)=f_m+\delta f_S$, and $\Delta F_{UN}-f_m\Delta x_{UN}=0$. It follows from Fig.1B in the text that $\tau_f\sim e^{f_Q\Delta x^{\ddagger}_{U\to N}/k_BT}$. Since f_S and f_Q are independent control variables in an experiment, one can factorize the survival probability as $\Sigma(t,f_S,f_Q)=\varphi_{UBA}(f_S)\Sigma(t;\infty,f_Q)$. Therefore,

$$\tau_F(\delta f_S,\delta f_Q)=\frac{\tau(0)}{1+e^{(-\delta f_S\Delta x_{UN})/k_BT}}e^{-\delta f_Q\Delta x^{\ddagger}_{U\to N}/k_BT} \tag{2}$$

where $\delta f_S=f_S-f_m$ and $\delta f_Q=f_m-f_Q$.

The expanding sausage model for a Gaussian chain under tension: In the presence of an external tension f, the simplest modification to the free energy of the expanding sausage model as a function of the length of the sausage ($\approx R$) is given by

$$F=\gamma A-fR\approx\frac{k_BT}{\xi^2}\times 2\pi\rho R-fR=\frac{k_BT}{\xi^2}2\sqrt{\pi\Omega}R^{1/2}-fR, \tag{3}$$

where the surface tension for the thermal blob (of size ξ) is given as k_BT/ξ^2, and the exposed surface area of the cylindrical sausage is $A\sim 2\pi\rho R$ (ρ is the radius of the sausage). The model is schematically shown in Fig. S4A. The rate of free energy reduction in the system is given by $\dot{F}=\gamma\dot{A}-f\dot{R}=\left(\frac{k_BT}{\xi^2}\sqrt{\pi\Omega}R^{-1/2}-f\right)\dot{R}$, while the entropy production due to the dissipation is $-T\dot{S}\approx\eta\times R\times\dot{R}^2$. Equating $\dot{F}=-T\dot{S}$, as in the main text, we obtain

$$t/\tau_0=\int_1^{R/R_0}\frac{x^{3/2}dx}{\overline{f}^0x^{1/2}-1}=\frac{2}{(\overline{f}^0)^5}\log\left(\frac{1-\overline{f}^0\left(\frac{R}{R_0}\right)^{1/2}}{1-\overline{f}^0}\right)-\sum_{k=1}^{4}\frac{2}{k(\overline{f}^0)^{5-k}}\left[1-\left(\frac{R}{R_0}\right)^{k/2}\right], \tag{4}$$

where R_0 the initial extension of the polymer, $\tau_0\equiv\frac{\eta\xi^2R_0^{5/2}}{k_BT\sqrt{\pi\Omega}}$, and $\overline{f}^0\equiv f\tau_0/\eta R_0^2$. The ratio R/R_0 in Eq.4 is interpreted as the survival probability [5], $P_S(t)$, as in the main text. For $\overline{f}^0\to 0$, we recover the de Gennes' collapse kinetics in poor solvent without tension, $P_S(t)=\left[1-\frac{5}{2}\left(\frac{t}{\tau_0}\right)\right]^{2/5}$. The average folding (collapse) time in the absence of tension, given in Eq. 6 of the main text, is $\langle\tau\rangle_0=\int_0^{2/5\times\tau_0}dtS_0(t)=\frac{2}{7}\tau_0$. Using the definition of τ_0 and $\overline{f}^0$, we can rewrite the free energy F in the dimensionless form, $\overline{F}\,(R/R_0)=\frac{F(R)\tau_0}{\eta R_0^3}=\left[2(R/R_0)^{1/2}-\overline{f}^0(R/R_0)\right]$, which is shown in Fig. S4A.

Above $\overline{f}^0=1$, the free energy develops a barrier ($\delta\overline{F}^{\ddagger}$) for refolding, whose position varies with force as $R^{TS}/R_0=1/(\overline{f}^0)^2$. If $R^{TS}<R_0$, a valid solution of SI Eq. 4 cannot be found for all $t>0$ (see also the discussion in the main text). The refolding time τ_F scales with the

effective height of a free energy barrier as $\tau_F \sim \exp(\delta F^{\ddagger})$ where $\delta F^{\ddagger}$ is easily calculated as $\delta\overline{F}^{\ddagger} = \overline{F}(R^{TS}/R_0) - \overline{F}(1) = 1/\overline{f}^0 - 2 + \overline{f}^0$. Therefore, the refolding (or nucleation) time scales with the quench force ($\overline{f}^0$) as

$$\tau_F \sim \exp\left[\frac{1}{\overline{f}^0} - 2 + \overline{f}^0\right], \tag{5}$$

in parallel to the calculation in the main text. The survival probability for varying $\overline{f}^0$ is shown in Fig. S4B. The average folding time is determined from Eq. 6, and we see in Fig. S4C that τ_F increases almost exponentially with the quench force for $\overline{f}^0 \lesssim 0.6$, beyond which there is a sharp increase in $\log[\tau_F(\overline{f}^0)]$. However, we note that the rapid reduction in R in the first stage of collapse seen in the simulations (Fig. 1D of the main text) is not observed in the predicted behavior of $R(t)/R_0$ for the Gaussian chain (Fig. S4B).

Barrier height in the WLC-expanding sausage model for $f_Q > (f_Q)^*$: When $\overline{f}_Q > (\overline{f}_Q)^*$, $R_0/L \to 1$ and $R^{TS}/L \to 0$. The conditions of $\overline{F}'(R_0/L) = 0$ and $\overline{F}'(R^{TS}/L) = 0$ i.e., $\overline{F}'(R_0/L) = 0 = (R_0/L)^{-1/2} + \overline{f}_p\left[1/4(1-R_0/L)^2 - 1/4 + R_0/L\right] - \overline{f}_Q \approx \overline{f}_p/4(1 - R_0/L)^2 - \overline{f}_Q$ and $\overline{F}'(R^{TS}/L) = 0 = \left(R^{TS}L\right)^{-1/2} + \overline{f}_p\left[1/4(1-R^{TS}/L)^2 - 1/4 + R^{TS}/L\right] - \overline{f}_Q \approx \left(R^{TS}/L\right)^{-1/2} - \overline{f}_Q$ lead to $R^{TS}/L \approx 1/\overline{f}_Q^2$ and $R_0/L \approx 1 - \frac{1}{2}\sqrt{\overline{f}_p/\overline{f}_Q}$. The free energy barrier for $\overline{f}_Q(> (\overline{f}_Q)^*)$ can be computed using

$$\begin{aligned}
\overline{F}(R^{TS}/L) &\approx \frac{1}{\overline{f}_Q} + \frac{\overline{f}_p}{4}\frac{1}{\overline{f}_Q^4}\left(\frac{3 - 2/\overline{f}_Q^2}{1 - 1/\overline{f}_Q^2}\right) \approx \frac{1}{\overline{f}_Q} + \frac{1}{4}\frac{\overline{f}_p}{\overline{f}_Q^4}\left(3 + \frac{1}{\overline{f}_Q^2} + \frac{1}{\overline{f}_Q^4} + \cdots\right) \\
\overline{F}(R_0/L) &\approx 2(1 - \sqrt{s} - \frac{s}{2} - \frac{s^{3/2}}{2} - \cdots) + \frac{\overline{f}_p}{4}\left(\frac{1}{2\sqrt{s}} - 6\sqrt{s} + 8s\right) - \overline{f}_Q(1 - 2s) \\
&= \frac{\overline{f}_p}{8\sqrt{s}} + (2 - \overline{f}_Q) - \left(2 - \overline{f}_Q + \frac{3}{2}\overline{f}_p\right)\sqrt{s} + 2\overline{f}_p s + \mathcal{O}(s^{3/2})\cdots
\end{aligned} \tag{6}$$

where $s(\equiv \overline{f}_p/\overline{f}_Q) \to 0$ when $\overline{f}_Q$ takes large value. Thus, the free energy barrier is calculated as

$$\begin{aligned}
\delta\overline{F}^{\ddagger} &= \overline{F}(R^{TS}/L) - \overline{F}(R_0/L) \\
&\approx \left(\frac{1 - 2\overline{f}_p^2}{\overline{f}_Q} - 2 + \overline{f}_Q\right) + \left(2 - \overline{f}_Q + \frac{3}{2}\overline{f}_p\right)\sqrt{\frac{\overline{f}_p}{\overline{f}_Q}} + \mathcal{O}\left[\left(\frac{\overline{f}_p}{\overline{f}_Q}\right)^{3/2}\right]
\end{aligned} \tag{7}$$

The collapse of a semiflexible chain in a poor solvent : The Hamiltonian used in our simulations of a wormlike chain in a poor solvent undergoing collapse to a toroidal structure upon force quench is given by

$$\mathcal{H} = \frac{k_s}{2a^2}\sum_{i=1}^{N-1}(r_{i,i+1}-a)^2 + \frac{k_b}{2}\sum_{i=1}^{N-2}(1-\hat{r}_i\cdot\hat{r}_{i+1}) + \epsilon_{LJ}\sum_{i,j}\left[\left(\frac{a}{r_{ij}}\right)^{12} - 2\left(\frac{a}{r_{ij}}\right)^{6}\right] - f(z_N - z_1)] \quad (8)$$

with the parameters, $\epsilon_{LJ} = 1.5k_BT$, $k_s = 2000k_BT$, $N = 200$, $a = 0.6$ and $k_b = 80$ k_BT. To integrate the equation of motion, we used Brownian dynamics algorithm $\vec{r}(t+\Delta t) = \vec{r}(t) - D\vec{\nabla}\mathcal{H}(\{\vec{r}\})\Delta t/k_BT + \vec{R}(t)$ where $\vec{R}(t)$ is a vector of Gaussian random number satisfying $\langle\vec{R}\rangle = 0$ and $\langle\vec{R}_\alpha(t)\cdot\vec{R}_\beta(t)\rangle = 2D\Delta t\delta_{\alpha\beta}$. We use diffusion coefficient $D = 1\times10^{-7}cm^2/s$, thus characteristic time for simulation is $a^2/2D \approx 2\ ns$. We chose integration time step $\Delta t = 0.00025(a^2/2D) \approx 0.5\ ps$.

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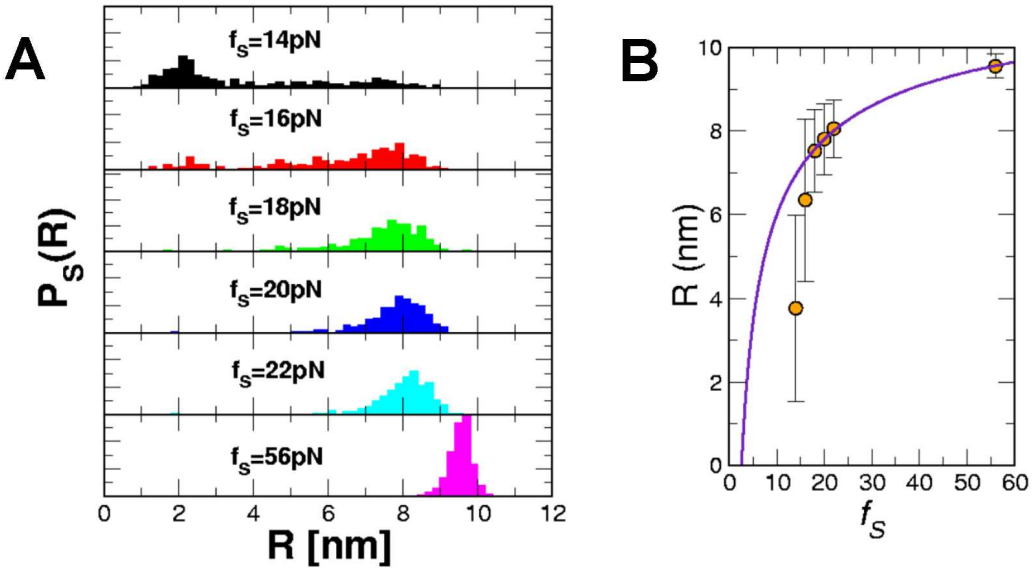

FIG. S1: Initial ensemble for the P5GA simulation. **A** Structural ensembles of the P5GA hairpin represented by $P(R)$ at each f_S. **B** The average end-to-end distance as a function f_S. Excluding the values at $f_S = 14$ and 16 pN, where the distribution is biomodal, $\langle R \rangle$ vs f_S is well fit by the wormlike chain model $\langle R \rangle \approx L\left(1 - \sqrt{\frac{k_B T}{4 l_p f_S}}\right)$, yielding $L = 12.2$ nm and $l_p = 0.43$ nm.

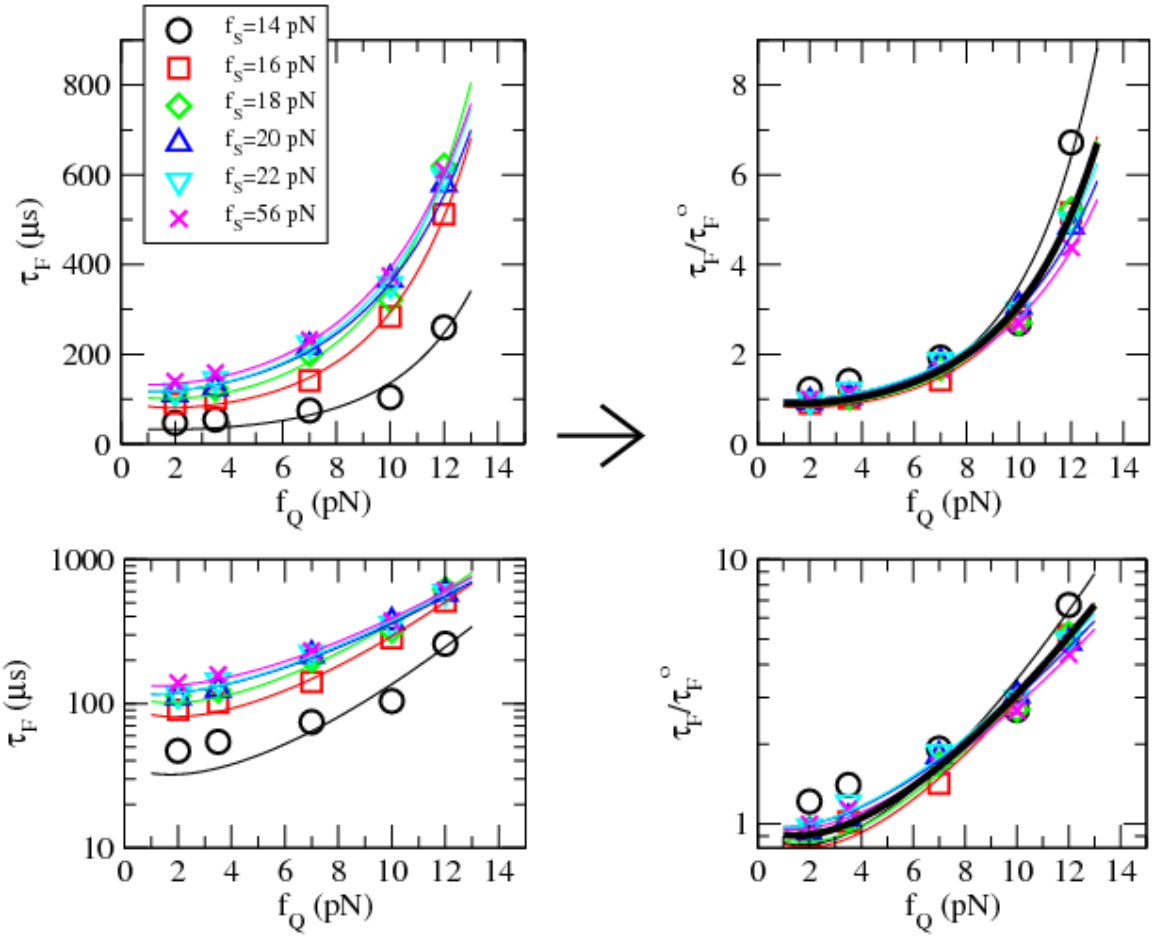

FIG. S2: Analysis of τ_F versus f_Q data by adapting Dudko and coworkers' microscopic model for force spectroscopy $\tau_F(f_Q, f_S) = \tau_F^o(f_S)\left(1+\frac{\nu f_Q \Delta x^{\ddagger}_{U\to F}}{\Delta F^{\ddagger}_{U\to F}}\right)^{1-1/\nu} e^{-\Delta F^{\ddagger}_{U\to F}/k_BT\cdot[1-(1+\nu f_Q \Delta x^{\ddagger}_{U\to F}/\Delta F^{\ddagger}_{U\to F})^{1/\nu}]}$ where we use $\nu = 2/3$ (cubic potential) and change the sign of force from the one in Ref.[6] to consider the refolding process under tension. When τ_F is scaled by τ_F^o for each f_S, the folding times approximately collapse to a single curve (right). From the fit using thick line, the parameters extracted for the collapsed data are $\Delta x^{\ddagger} = 0.45$ nm and $\Delta F^{\ddagger}_{U\to F} = 0.56\ pN \cdot nm$.

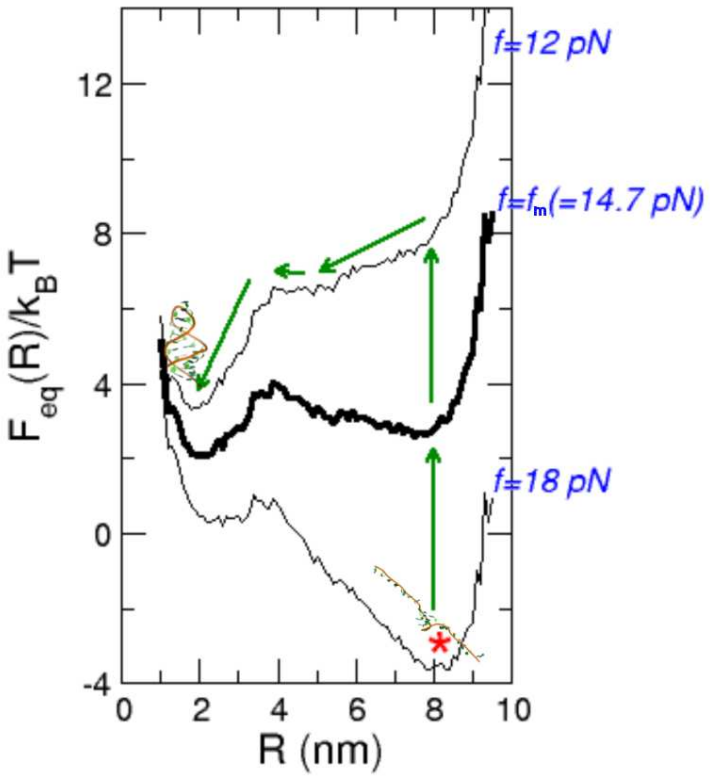

FIG. S3: The free energy of the P5GA hairpin as a function of R near $f = f_m$, schematically illustrating how the initially stretched structure of RNA at $f_S = 18$ pN adapts its structure under the force-quench condition at $f_Q = 12$ pN.

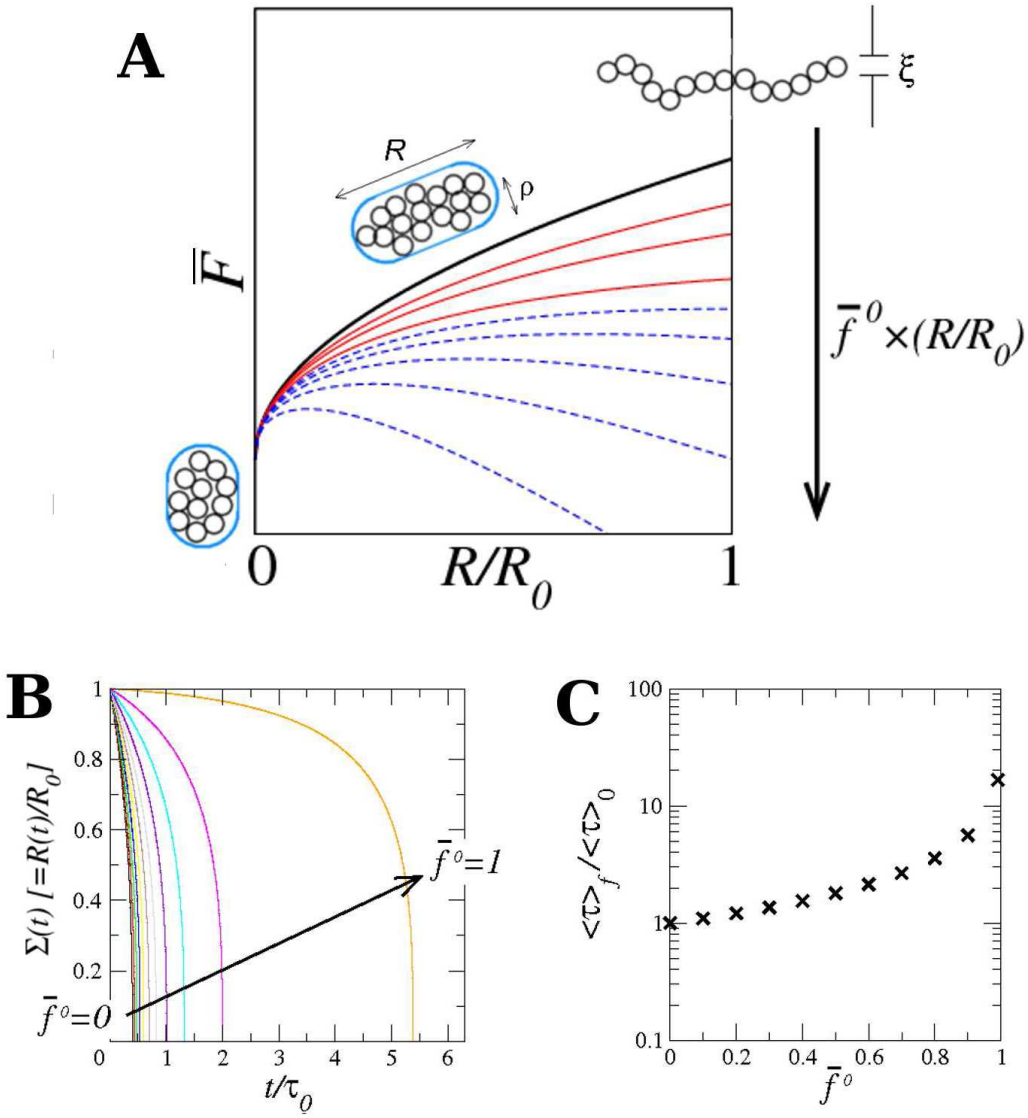

FIG. S4: The expanding sausage model under variation of the external tension. **A**. The free energy profile calculated using R/R_0 with varying tension (f_Q). The collapse of a homopolymer is diagrammed schematically for $f_Q = 0$, but the extended structure can be stabilized in the presence of tension. **B**. Reduction of the molecular extension with increasing tension (from left to right). **C**. The average refolding time as a function of external tension, with $\log(\tau_F) \sim \overline{f}^0$ for $\overline{f}^0 \lesssim 0.6$.

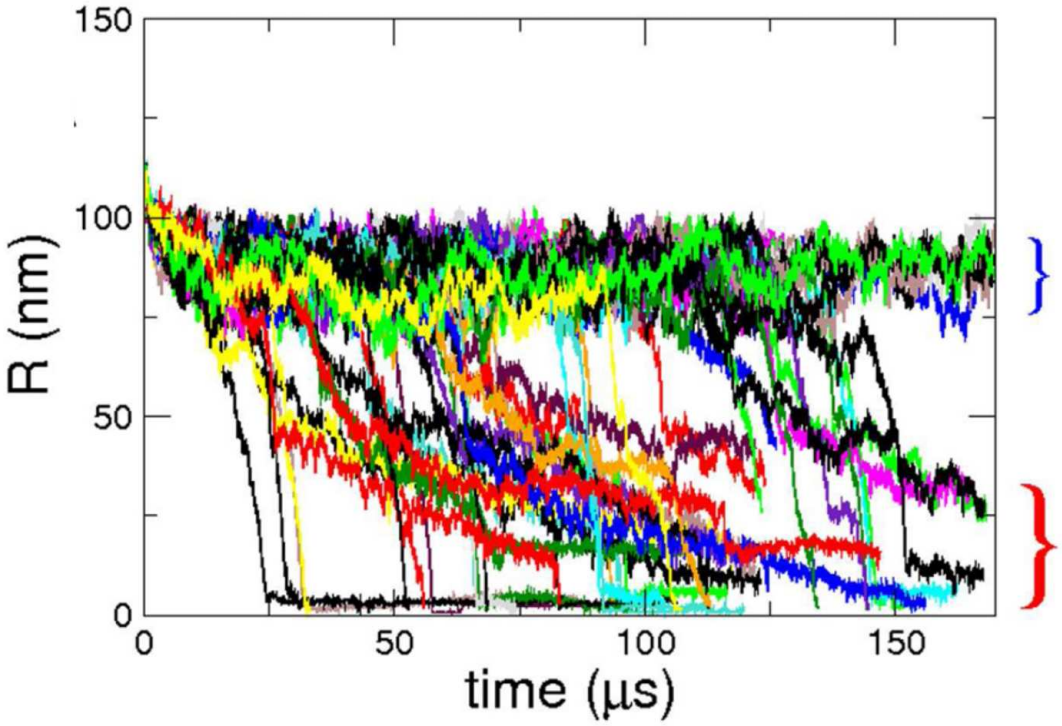

FIG. S5: Full 50 force-quench induced dynamic trajectories of semiflexible polymers.

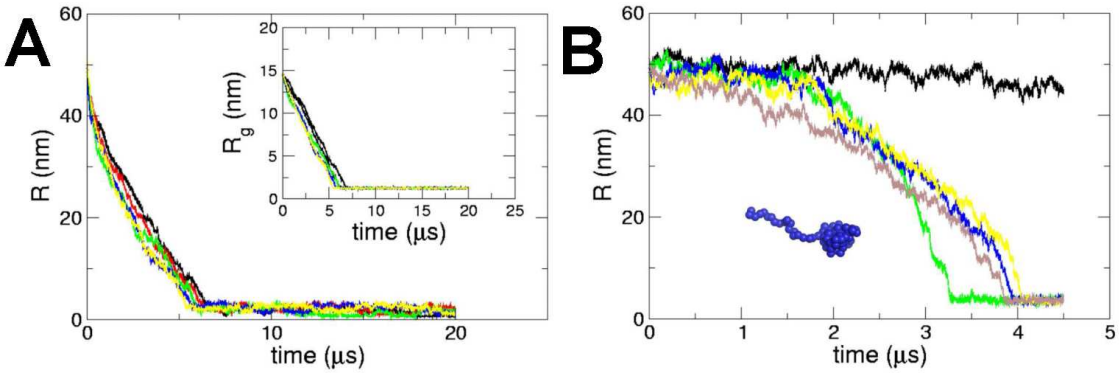

FIG. S6: The collapse dynamics of a freely jointed homopolymer in a poor solvent is shown, with $f_S = 83$ pN to $f_Q = 4$ pN (**A**) and $f_S = 83$ pN to $f_Q = 75$ pN (**B**). The flexible chain shows no evidence of the plateau for small f_Q, but a higher quench force stabilizes intermediate structures.