Supplementary Information:
Determining Elasticity from Single Polymer Dynamics

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Supplementary data
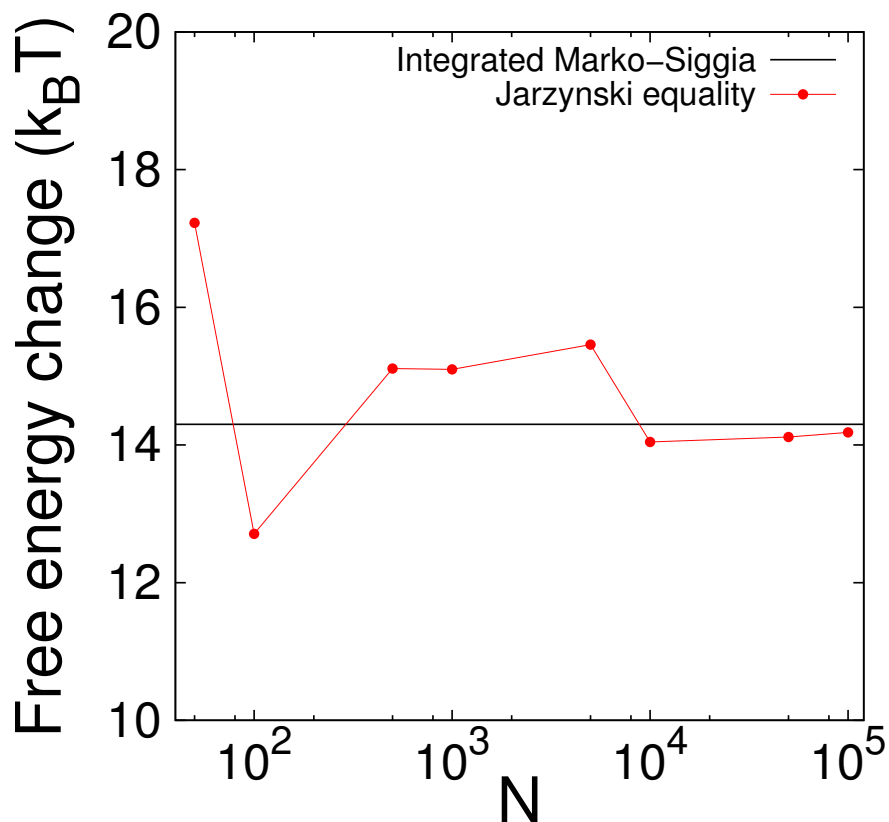

Fig. S1. Convergence of Jarzynski equality in estimating free energy change as a function of number of molecules N used in ensemble for $\lambda - DNA$ (contour length $\approx 21~\mu$m) in extensional flow, where the polymer is modeled as a single mode dumbbell. Polymers are stretched from fractional extension of ≈ 0.32 to 0.38. The horizontal line represents analytical estimate from integrating the Marko-Siggia force relation.
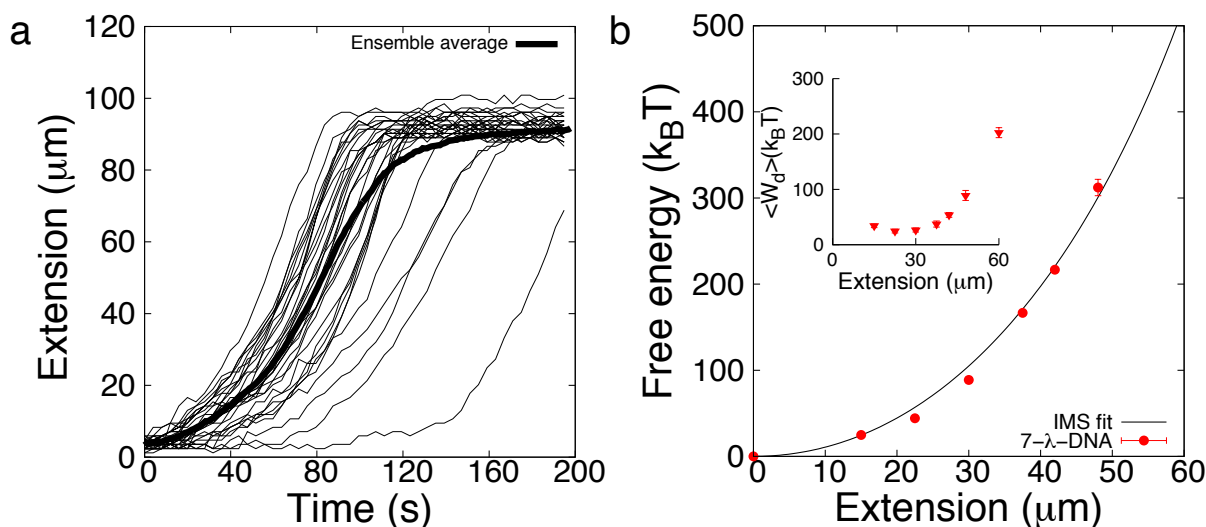
Fig. S2. Application of the nonequilibrium framework to experimental data on polymer stretching dynamics in extensional flow. (a) Individual (light) and ensemble average (dark) stretching trajectories of 7-λ-DNA molecules in extensional flow at $Wi = 0.98$. (b) Molecular free energy landscape determined from applying JE to experimental stretching trajectories. Solid line is the integrated Marko-Siggia (IMS) relation with contour length as fitting parameter. (Inset) Average dissipated work as a function of molecular extension. Data shown are mean values ± SD.

Supplementary text

Derivation for rate of work

In order to calculate the work done by the fluid on stretching a polymer molecule, the rate of work needs to be determined. Considering the hydrodynamic drag on a polymer chain, there are two "limits" or stretching regimes for a polymer stretching in flow.[1] In the coiled conformation (or Zimm regime), the chain behaves as a random coil with a constant drag coefficient ζ.[2] Zimm theory is applicable in this regime as suggested by experimental diffusion data for single DNA molecules of comparable size.[3] The second regime is the stretched state of a polymer chain, where a polymer chain behaves as a slender body with a drag coefficient that increases approximately linearly with chain extension. Several prior publications have confirmed that slender body theory is reasonably applicable for polymers stretched in extensional flow, where a chain extends along the extensional flow axis an the flow has zero vorticity[1,4]. In this regime, we invoke slender body relation for hydrodynamic drag by analyzing single molecule images of DNA molecules stretched in flow, which allows for calculation of the projected chain extension in flow. Using this approach, we determined the work rate as a function of chain extension.

Coiled conformation (Zimm regime)

Here, we treat the polymer molecule as sphere of size R_g, where R_g is the radius of gyration of the molecule, with a constant drag coefficient ζ. The drag force on the molecule is then given by $\mathbf{F}^{drag} = \zeta\mathbf{u}$, where $\mathbf{u}$ is the unperturbed fluid velocity. In a planar extensional flow, the unperturbed fluid velocity is given as $\mathbf{u} = \dot{\epsilon}[x, -y]$ in cartesian coordinates, where $\dot{\epsilon}$ is the applied strain rate. For convenience, we switch to spherical coordinates such that $\mathbf{u} = \dot{\epsilon}R_g\sin\theta[\cos\phi, -\sin\phi]$. Using this coordinate, the work rate $\dot{w}$ for the sphere is then given by $\int d\Omega\mathbf{u}\cdot\mathbf{F}^{drag}$, where the integral is over the the differential solid angle $d\Omega = \sin\theta d\theta d\phi$. Based on this analysis, the work rate for the sphere

is:

$$\dot{w} = \int_{\phi=0}^{2\pi} \int_{\theta=0}^{\pi} \zeta \dot{\epsilon}^2 R_g^2 \sin^3 \theta \, \mathrm{d}\theta \mathrm{d}\phi = \frac{8}{3} \pi \zeta \dot{\epsilon}^2 R_g^2. \tag{1}$$

For the purpose of experimental analysis, we express the work rate in terms of end-to-end extension x (obtained from single molecule measurements) by using the fact that $R_g = x/\sqrt{6}$ for linear chains. Therefore, the work rate $\dot{w} = \frac{4}{9} \pi \zeta \dot{\epsilon}^2 x^2$.

Stretched conformation (slender body regime)

Here, we treat the polymer molecule as slender body of length x and diameter d, where x is the end-to-end extension of the molecule and d is the molecular diameter of DNA $= 2nm$. Slender body theory predicts that the drag force on a body suspended in a fluid in uniform flow at the velocity u is given as $F^{drag} = \frac{2\pi\eta_s x}{\ln(x/d)} u$, where η_s is the solvent viscosity. Therefore, for a slender body in a planar extensional flow, the drag force on a differential element $\mathrm{d}s$ of a slender body $\mathrm{d}F^{drag} = \frac{2\pi\eta_s \dot{\epsilon} s \mathrm{d}s}{\ln(x/d)}$.[5] Furthermore, the work rate is given by $\int u \mathrm{d}F^{drag}$. Using this approach, the work rate for a slender body is:

$$\dot{w} = \int_{s=-\frac{x}{2}}^{\frac{x}{2}} \frac{2\pi\eta_s \dot{\epsilon}^2 s^2}{\ln(x/d)} \mathrm{d}s = \frac{1}{6} \pi \eta_s \dot{\epsilon}^2 \frac{x^3}{\ln(x/d)}. \tag{2}$$

The work done by the fluid on the molecule is then determined by integrating the work rate from time zero (at zero flow) to the time required to reach a final extension.

Transition between regimes

The transition between the Zimm regime and the slender body regime is determined by finding the extension at which the work rates in the coiled and stretched configurations are equal. Specifically, the crossover extension corresponds to the chain extension where equations (1) and (2) are equal. From our analysis, the crossover extension depends only on ζ and is found to be ≈ 8 μm for the parameters used in this study, which is in good agreement with large-scale Brownian dynamics simulations with multi-body hydrodynamic interactions.[1]

Model discretization and free energy calculations

To validate our framework, we studied the effect of model discretization on free energy calculations using the JE for polymeric systems driven by external flows. We performed a systematic study of the effect of coarse graining on JE calculations for mesoscopic bead-spring chains commonly used in BD simulations of polymers. We modeled λ-DNA with varying levels of discretization while maintaining the contour length L of the chain constant. Work distributions for each level of discretization and the corresponding free-energy landscape obtained via JE are shown in Fig. S3. Importantly, we observed that the JE yields accurate results for mesoscopic models of polymers (within a few $k_B T$), independent of the level of discretization for models ranging from a simple dumbbell to multi-bead spring chains. We found that finer levels of discretization allowed for the use of fewer molecules in an ensemble (up to an order of magnitude less) required to obtain the free-energy landscape, whereas higher levels of discretization allow for more coarse stratification schemes.
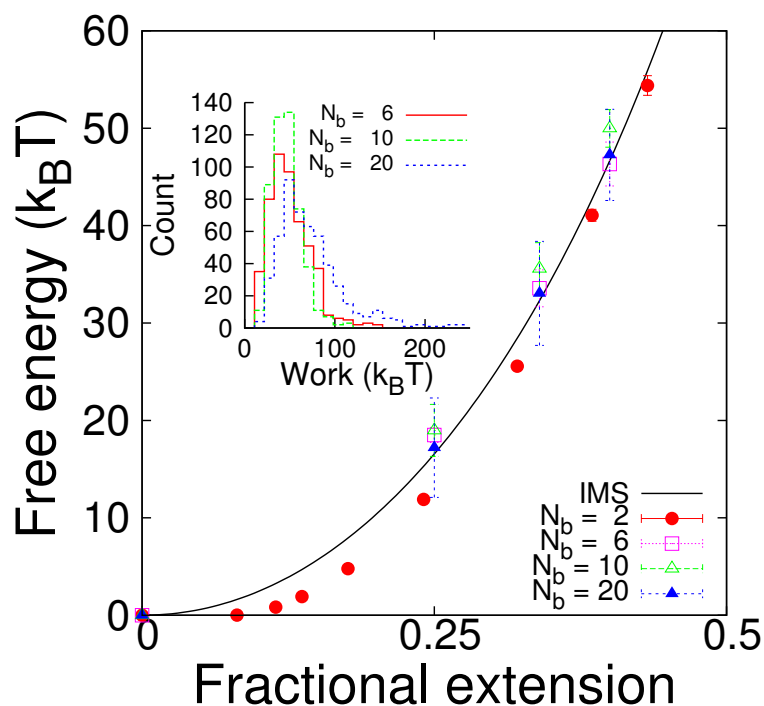
Fig. S3. Free-energy landscape of λ-DNA determined by applying the JE with varying levels of chain discretization $N_b = 6, 10, 20$. IMS: integrated Marko-Siggia relation. Mean $\pm$ SD of free-energy landscape are shown for finer levels of discretizations. (Inset) Work distributions for varying levels of coarse-graining for λ-DNA in extensional flow.

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[5] Larson, R. G. Principles for coarse-graining polymer molecules in simulations of polymer fluid mechanics. *Mol. Phys.* **102**(4), 341–351 (2004).