

Thermodynamics of single molecule stretching

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- Do thermodynamics apply to small systems?
- Many oppose that a e.g. Gibbs-Duhem relationship is applicable for single molecular systems¹
- May have a large fundamental impact on how one can describe biomolecular and other events related to energy conversion on the small scale.
- The aim of the project is to verify the rate laws presented by Rubi et al.²

¹David Keller, David Swigon, and Carlos Bustamante. "Relating Single-Molecule Measurements to Thermodynamics". In: *Biophysical Journal* 84. February (2003), pp. 733–738.

²J M Rubi, D Bedeaux, and S Kjelstrup. "Thermodynamics for Single-Molecule Stretching Experiments". In: *Journal of computational chemistry* 110.25 (2006), pp. 12733–12737.



- Motivation
- Background
- Model and method
- Previous work
- Free energy estimation
- Rate laws and entropy production
- Conclusion

The rate laws

There is a friction coefficient associated with an increment of either stretching velocity v or the constraining force f .

In the Helmholtz ensemble (length controlled)

$$\Delta \bar{f} = \xi_l(l)v, \quad (1)$$

and in the Gibbs ensemble (force controlled)

$$\Delta f = \xi_f(f)\bar{v}. \quad (2)$$

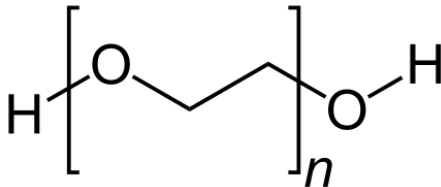
Hill's theory for small system thermodynamics³

- An equilibrium description of thermodynamic properties on the nano-scale.
- The thermodynamic functions cease to be extensive at this length scale.
- Hill introduced an ensemble of small systems, and used the replica energy to obtain thermodynamic properties that depended on the surface area and curvatures.
- The choice of ensemble will affect the thermodynamic potentials for small systems.

³Terrell L. Hill. *Thermodynamics of Small Systems*. New York: W.A. Benjamin Inc, 1963, p. 210.

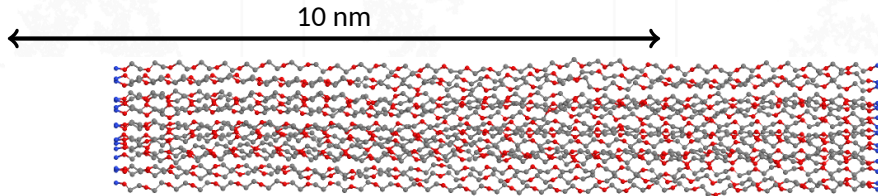
Polyethylene oxide (PEO)

- It is studied extensively experimentally.
- Applications ranging from industrial manufacturing to medicine.
- A better understanding of the mechanical properties of PEO on the nano-scales is needed.



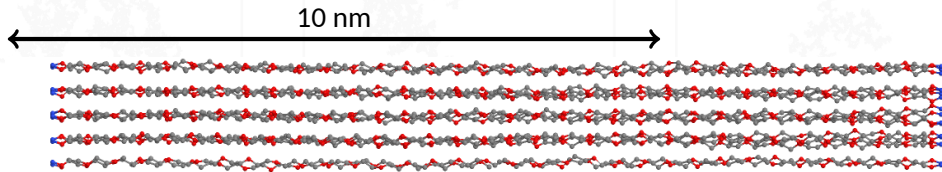


Previous work: Breaking of bundles



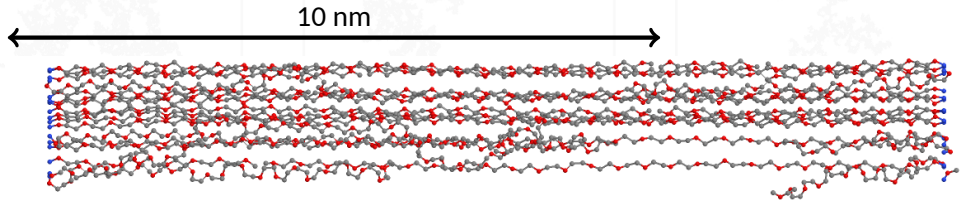


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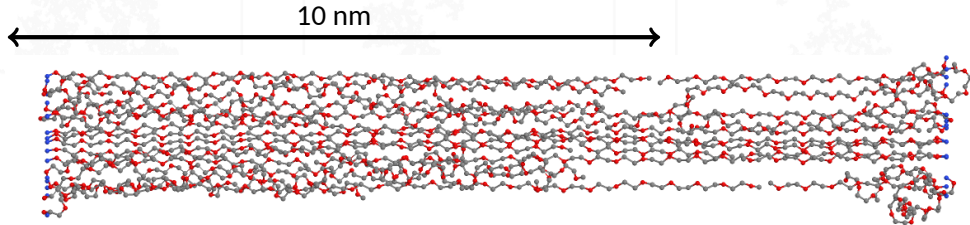


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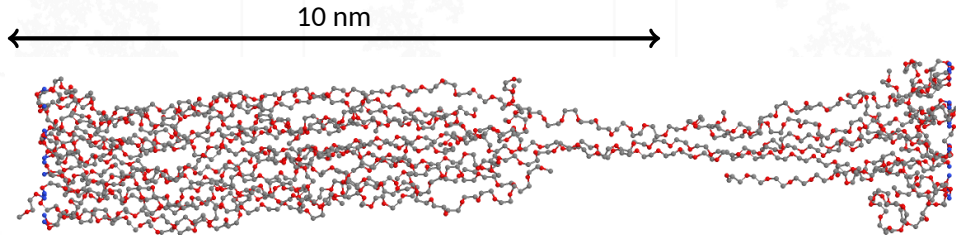


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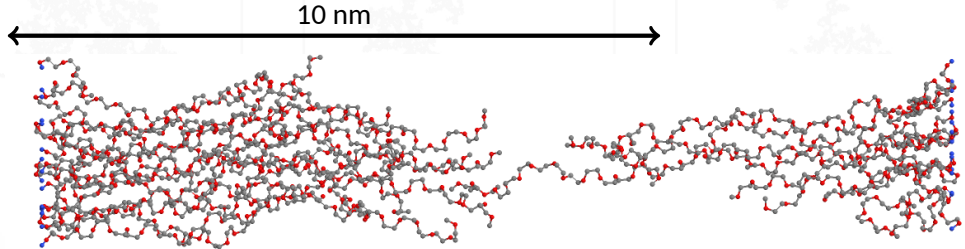


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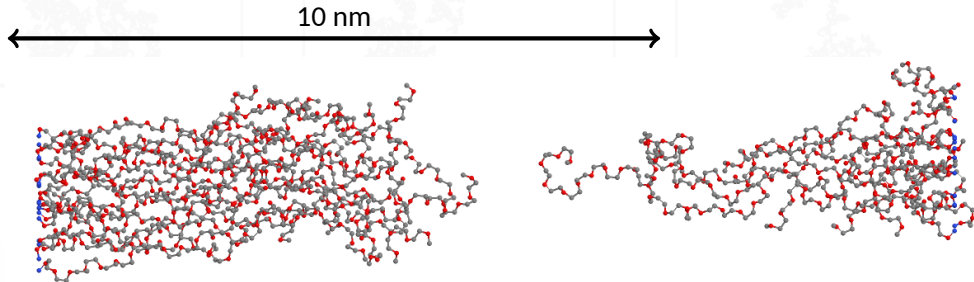




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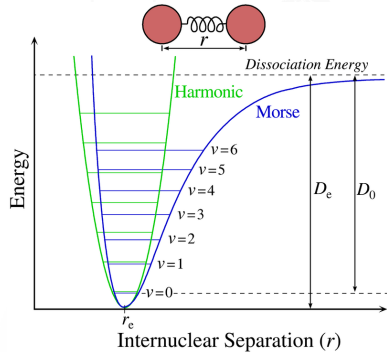
Previous work: Breaking of bundles





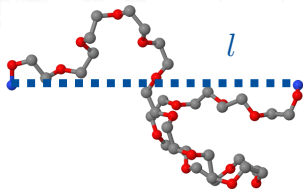
Simulation details

- United atom force field
- Stretching, bending, torsion
- Langevin thermostat at $T=200$ K

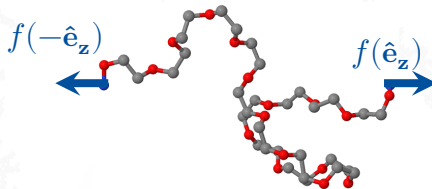


Two ensembles

Helmholtz ensemble (isometric)



Gibbs ensemble (isotensional)



Model validation using the entropic regime

The entropy in the molecule is given by

$$S(l) - S_0 = -\frac{3}{2}k_B l^2 / R_g^2 \quad (3)$$

giving rise to an entropic force f_s of

$$f_s = -\frac{\partial(S(l)T)}{\partial l} = 3k_B T l / R_g^2. \quad (4)$$

In the entropic region the molecule follows a random walk in three dimensions. If we let the molecule be composed of N_{eff} independent units of length b_{eff} , the radius of gyration reads

$$R_g = \frac{l_{\text{ext}}}{\sqrt{6N_{\text{eff}}}}, \quad (5)$$

where $l_{\text{ext}} = N_{\text{eff}} b_{\text{eff}}$ is length of the fully extended molecule.

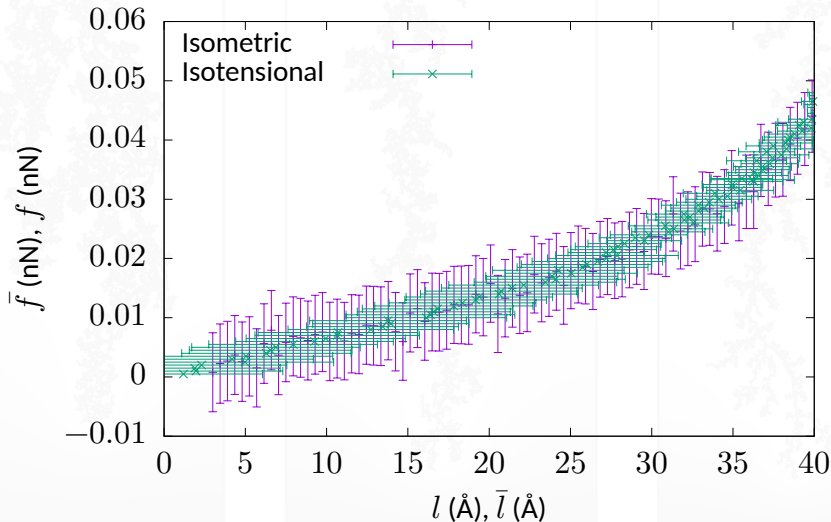
Model validation using the entropic regime

This gives an effective entropic force of

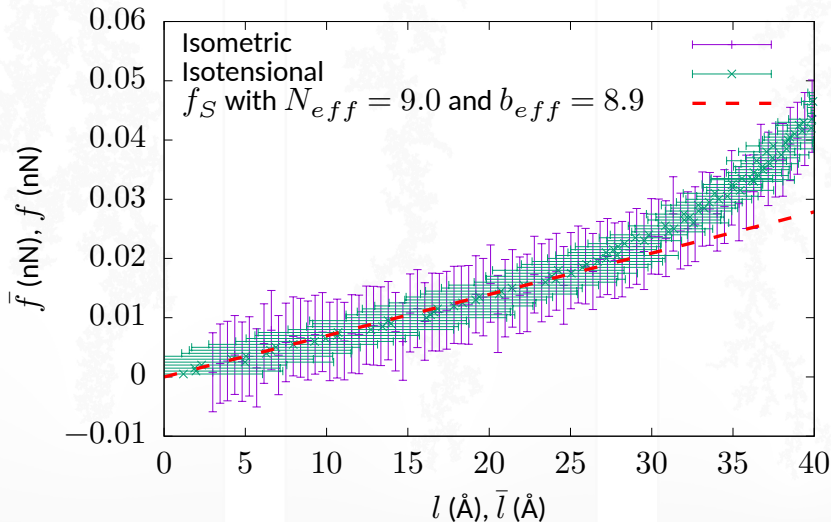
$$f_s = \frac{18k_B T l N_{\text{eff}}}{l_{\text{ext}}^2} \quad (6)$$

The number of independent units depends on the system size, whereas the effective length b_{eff} should be size independent.

Model validation using the entropic regime



Model validation using the entropic regime



Estimation of free energy

For the isometric simulations, there is a fluctuating force for each length. If we let

$$\langle f(t) \rangle_l = \bar{f}(l), \quad (7)$$

the Helmholtz energy is given by

$$A(l) = \int_{l_0}^l \bar{f}(l') dl'. \quad (8)$$

For the isotensional simulations there is a fluctuating length for each force. If we let

$$\langle l(t) \rangle_f = \bar{l}(f), \quad (9)$$

the Gibbs free energy is given by

$$G(f) = \int_{f_0}^f \bar{l}(f') df'. \quad (10)$$

Estimation of free energy

In the thermodynamical limit A and G are related by a Legendre transformation, and with $\Delta l = l - l_0$ and $\Delta \bar{f} = \bar{f}(l) - \bar{f}(l_0)$ one has

$$A(l) + G(f = \bar{f}(l)) = \Delta \bar{f} \Delta l \quad (11)$$

for sufficiently large systems⁴.

⁴J M Rubi, D Bedeaux, and S Kjelstrup. "Thermodynamics for Single-Molecule Stretching Experiments". In: *Journal of computational chemistry* 110.25 (2006), pp. 12733–12737.

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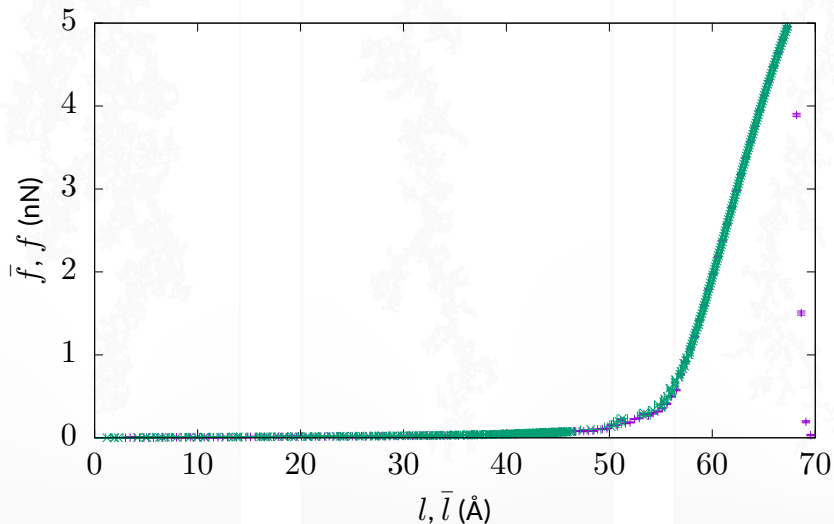
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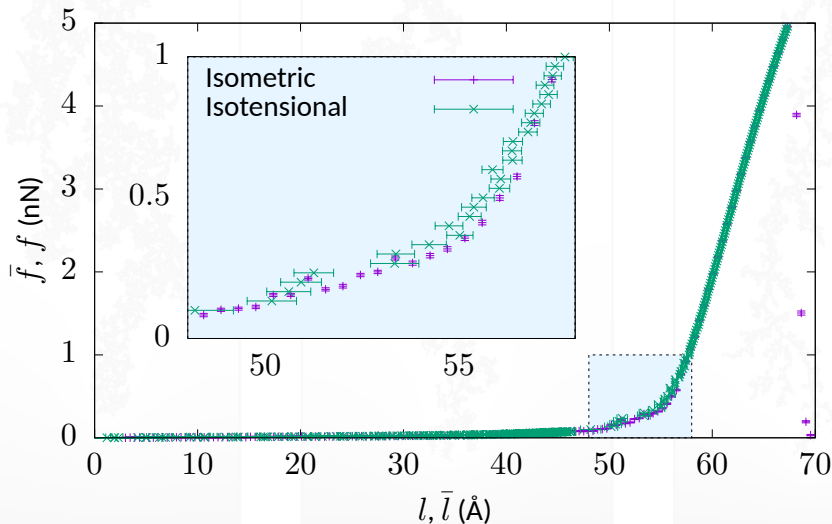
Let us investigate how this is for a PEO chain of $N = 51$ units.

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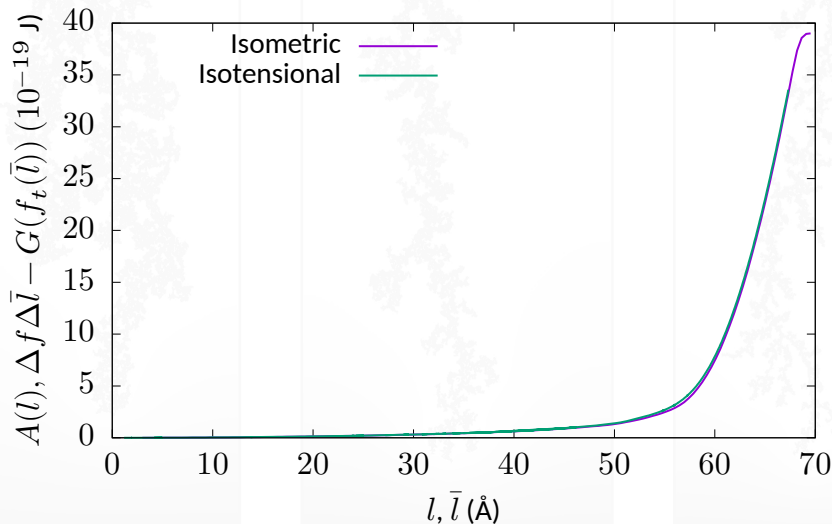
Force-elongation



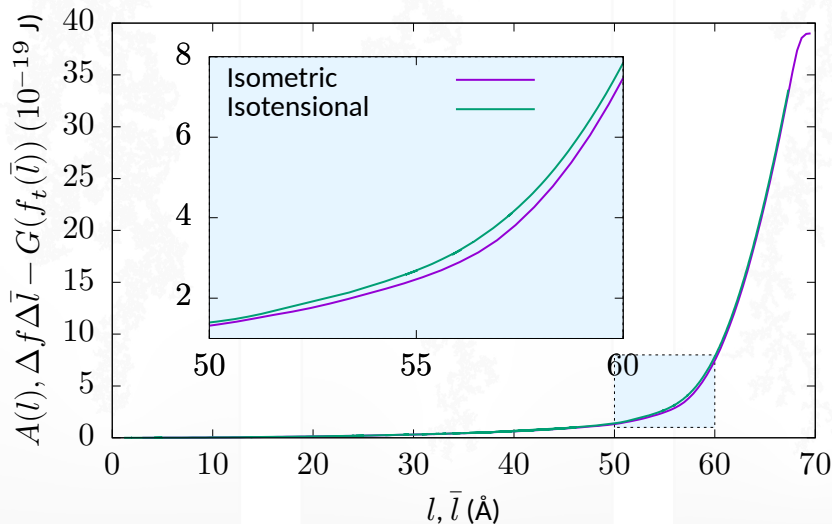
Force-elongation



Estimation of free energy



Estimation of free energy



Entropy production

When changing the controlled force from f to f_{ext} , the entropy production have previously been shown to be⁵

$$\frac{dS}{dt} = \frac{1}{T} (f_{ext} - f) \frac{d\bar{l}}{dt}. \quad (12)$$

With $\Delta f = f_{ext} - f$, the resulting force controlled rate law is

$$\Delta f = \xi_f(f) \frac{d\bar{l}}{dt} \equiv \xi_f(f) \bar{v}, \quad (13)$$

where $\xi_f = \xi_f(f)$ is the isotensional friction coefficient and \bar{v} the resulting average stretching velocity.

⁵ J M Rubi, D Bedeaux, and S Kjelstrup. "Thermodynamics for Single-Molecule Stretching Experiments". In: *Journal of computational chemistry* 110.25 (2006), pp. 12733–12737.

The entropy production associated with increasing the length of the molecule at a constant velocity $v = \frac{dl}{dt}$ is given by

$$\frac{dS}{dt} = \frac{1}{T}(\bar{f}_{ext} - \bar{f})\frac{dl}{dt} \equiv \xi_l(l)v, \quad (14)$$

and with $\Delta\bar{f} = \bar{f}_{ext} - \bar{f}$ as the velocity induced force change, the length controlled rate law is

$$\Delta\bar{f} = \xi_l(l)\frac{dl}{dt} \equiv \xi_l(l)v, \quad (15)$$

Force controlled rate law

Our first aim is to determine the force controlled rate law:

$$\Delta f = \xi_f(f) \bar{v}. \quad (16)$$

The samples are equilibrated for 5 ns at a fixed force before the force is increased by a step of Δf

Force controlled rate law

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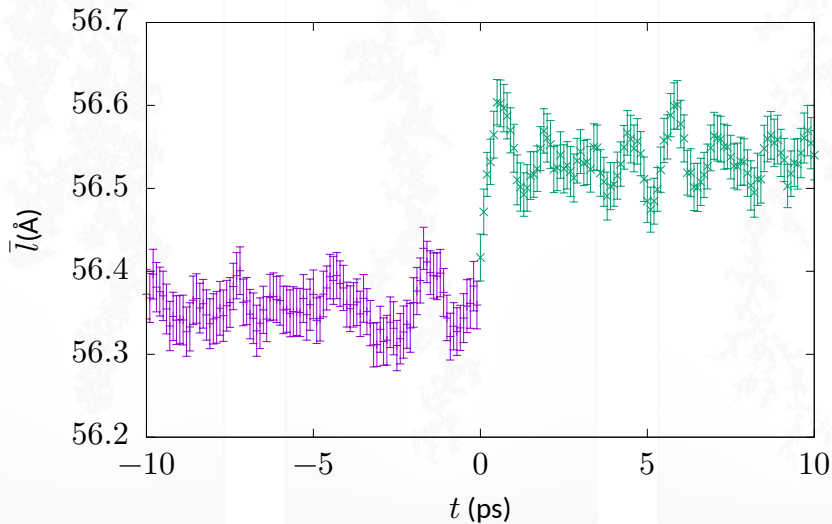
$$\Delta f = \xi_f(f) \bar{v}. \quad (16)$$

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Let us look at the average length as a function of time for samples equilibrated at $f_0 = 0.67$ nN when we increase the force by 8% at $t = 0$.

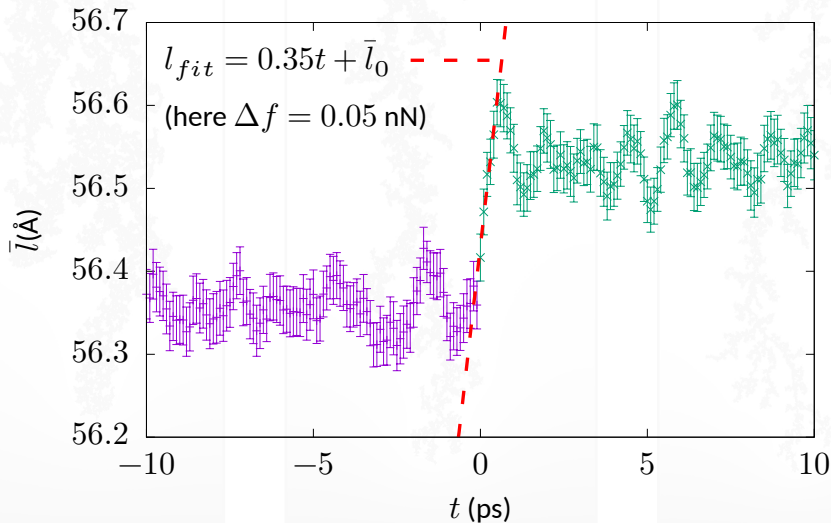
Force controlled simulations:

$$\Delta f = \xi_f(f) \bar{v}$$



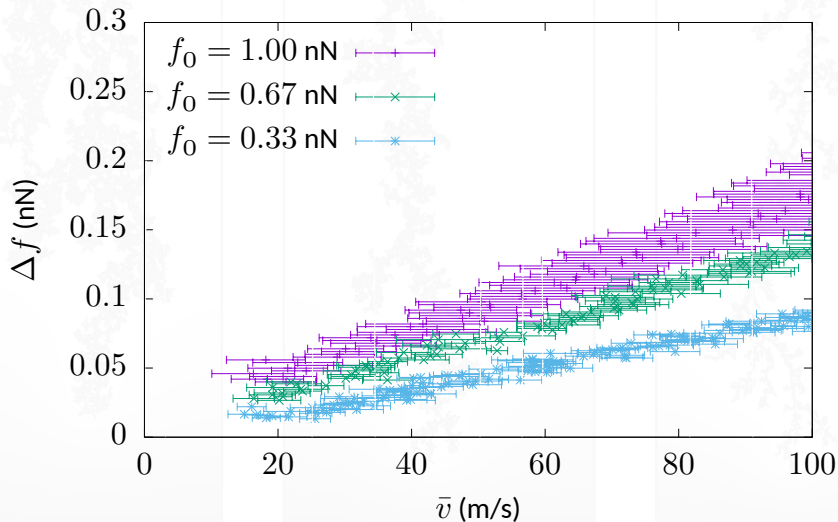
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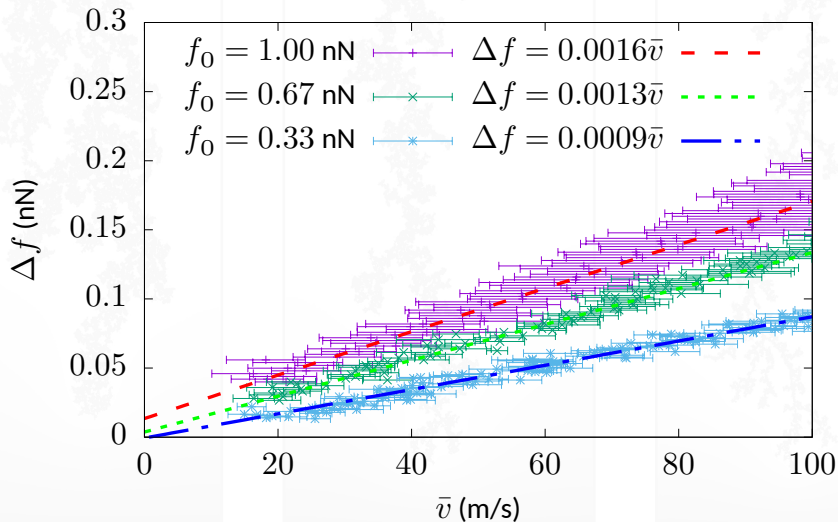
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$$\Delta \bar{f} = \xi_l(l)v. \quad (17)$$

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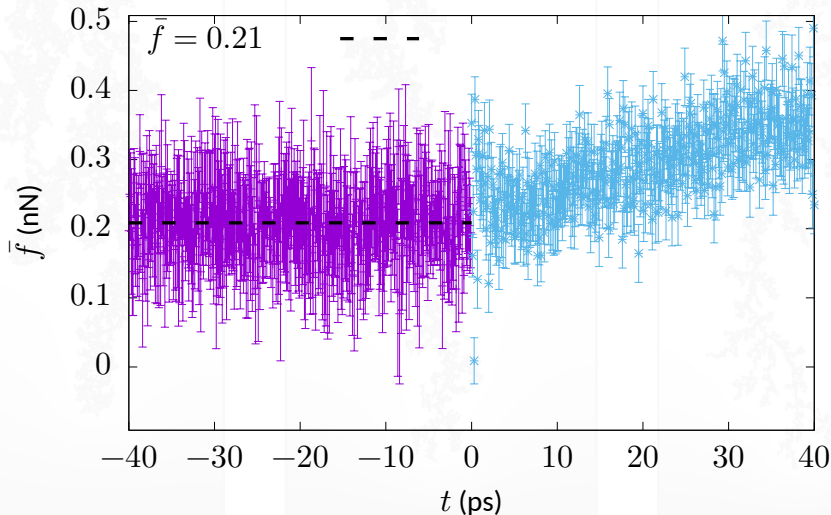
$$\Delta \bar{f} = \xi_l(l)v. \quad (17)$$

The samples are equilibrated for 5 ns at a fixed length before the length is increased at a constant velocity.

Let us look at the average force as a function of time for samples equilibrated at $l_0 = 52 \text{ \AA}$ when we stretch the molecule at a constant velocity $v = 4 \text{ m/s}$ from $t = 0$.

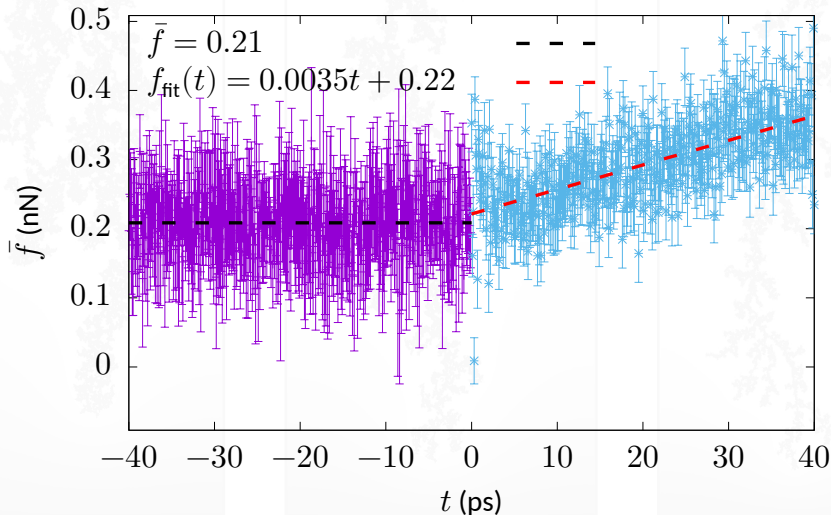
length controlled simulations:

$$\Delta \bar{f} = \xi_l(l)v$$



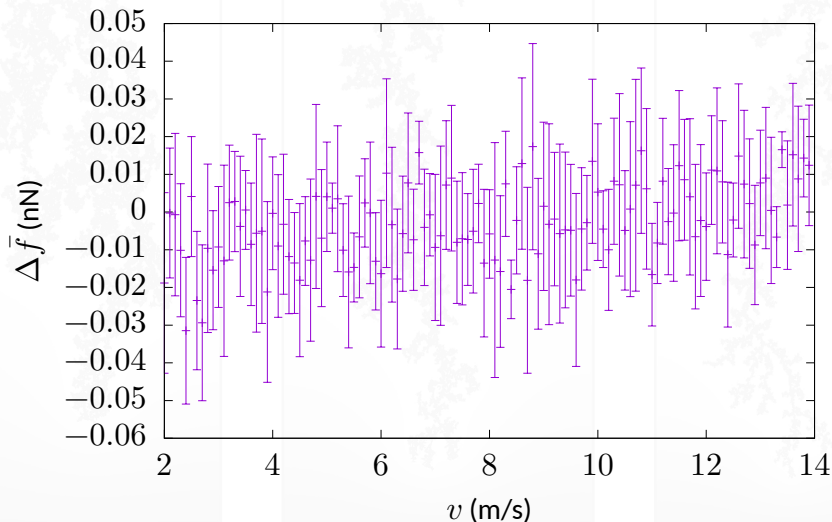
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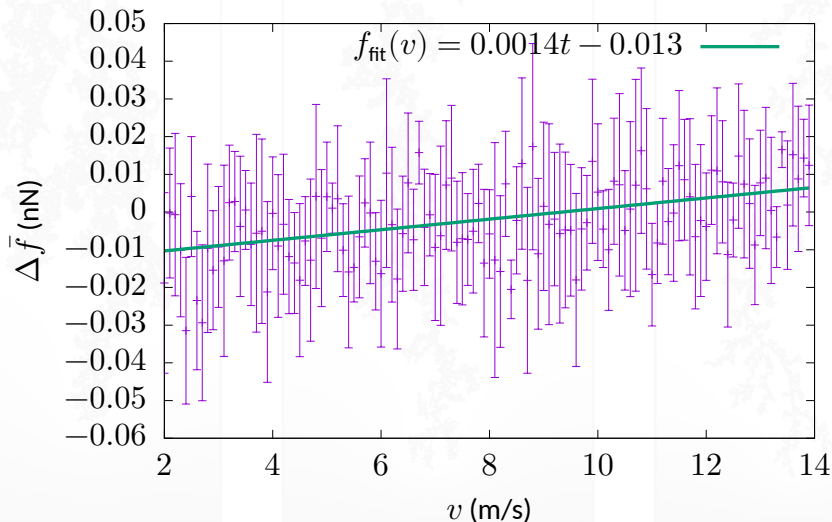
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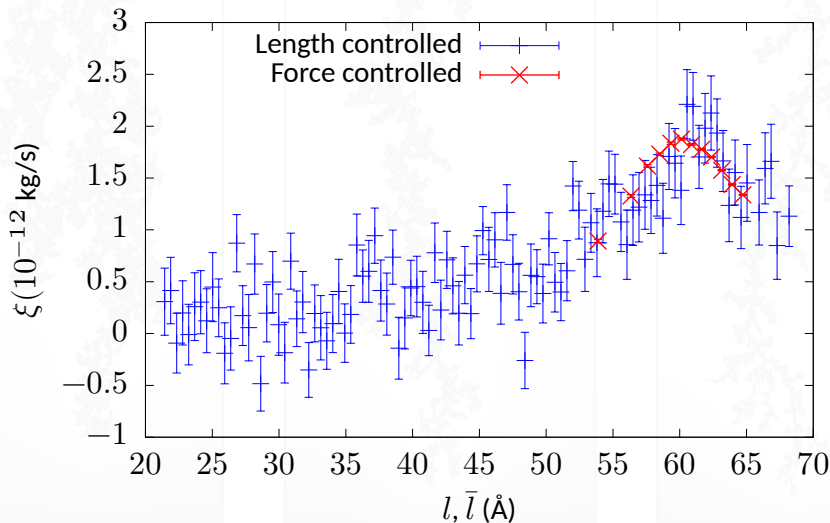


length controlled simulations:

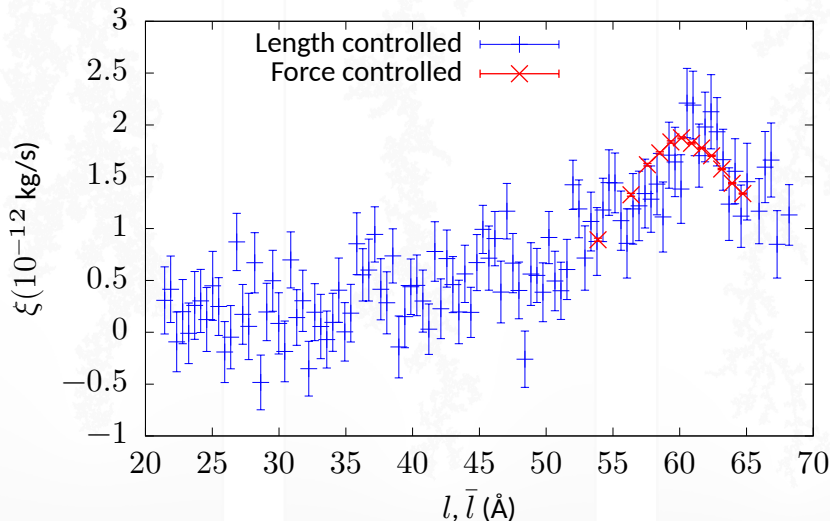
$$\Delta \bar{f} = \xi_l(l)v$$



Friction coefficients



Entropy production at $v = 14$ m/s



Conclusion

- Nanometric chains of PEO have been analyzed in the Helmholtz and Gibbs ensemble by non-equilibrium molecular dynamic simulations.

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- They still tell a coherent story in agreement with the rate laws presented by Rubi et al.⁶

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- On this length scale, the thermodynamic potentials are ensemble dependent
- They still tell a coherent story in agreement with the rate laws presented by Rubi et al.⁶
- A thermodynamic description is meaningful also on the small scale.

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Thank you!

