Thermodynamics of single molecule stretching

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Motivation

- Do thermodynamics apply to small systems?
- Many oppose that a e.g. Gibbs-Duhem relationship is applicable for single molecular systems.\(^1\)
- 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.\(^2\)

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• 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)

$$\Delta \bar{f} = \bar{\xi}_l(l)v,$$  \hspace{1cm} (1)

and in the Gibbs ensemble (force controlled)

$$\Delta f = \bar{\xi}_f(f)\bar{v}.$$ \hspace{1cm} (2)
Hill’s theory for small system thermodynamics

- 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.

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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.

![PEO structural formula](image)
Previous work: Breaking of bundles
Previous work: Breaking of bundles

10 nm
Previous work: Breaking of bundles

10 nm
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10 nm
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10 nm
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10 nm
Previous work: Breaking of bundles

10 nm
Simulation details

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

Helmholtz ensemble (isometric)  
Gibbs ensemble (isotensional)
The entropy in the molecule is given by

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

giving rise to an entropic force \( f_s \) of

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

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

\[ R_g = \frac{l_{\text{ext}}}{\sqrt{6 N_{\text{eff}}}}. \] (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

\[ f_s = \frac{18 k_B T l N_{\text{eff}}}{l_{\text{ext}}^2} \]  \hspace{1cm} (6)

The number of independent units depends on the system size, whereas the effective length \( b_{\text{eff}} \) should be size independent.
Model validation using the entropic regime

\[ \bar{f}(\text{nN}), f(\text{nN}) \]

Isometric
Isotensional
Model validation using the entropic regime

Isometric
Isotensional
$f_S$ with $N_{eff} = 9.0$ and $b_{eff} = 8.9$
For the isometric simulations, there is a fluctuating force for each length. If we let
\[ \langle f(t) \rangle_l = \bar{f}(l), \] (7)
the Helmholtz energy is given by
\[ A(l) = \int_{l_0}^{l} \bar{f}(l') dl'. \] (8)

For the isotensional simulations there is a fluctuating length for each force. If we let
\[ \langle l(t) \rangle_f = \bar{l}(f), \] (9)
the Gibbs free energy is given by
\[ G(f) = \int_{f_0}^{f} \bar{l}(f') df'. \] (10)
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

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

(11)

for sufficiently large systems$^4$.

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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 \( \Delta \tilde{f} = \tilde{f}(l) - \tilde{f}(l_0) \) one has

\[
A(l) + G(f = \tilde{f}(l)) = \Delta \tilde{f} \Delta l
\]

(11)

for sufficiently large systems\(^4\).

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

Force-elongation

\[ f, f \text{ (nN)} \]

\[ l, \bar{l} \text{ (Å)} \]
Force-elongation

Isometric
Isotensional

\[ f, \bar{f} \text{ (mN)} \]

\[ l, \bar{l} \text{ (Å)} \]
Estimation of free energy

\[ A(l), \Delta f \Delta l - G(f_t(l)) (10^{-19} J) \]

Graph showing the relationship between \( l, \bar{l} \) (Å) and the free energy expression.
Estimation of free energy

\[ A(l), \Delta f \Delta \bar{l} - G(f_\bar{t})(10^{-19} J) \]

Isometric
Isotensional
When changing the controlled force from $f$ to $f_{\text{ext}}$, the entropy production have previously been shown to be:

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

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

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

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

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Entropy

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

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

(14)

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

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

(15)
Our first aim is to determine the force controlled rate law:

\[ \Delta f = \xi_f(f)\bar{v}. \]  \hspace{1cm} (16)

The samples are equilibrated for 5 ns at a fixed force before the force is increased by a step of \( \Delta f \).
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 $\Delta f$.

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:

\[ \Delta f = \xi_f(f) \bar{v} \]
Force controlled simulations:

\[ \Delta f = \xi_f(f) \bar{v} \]

\[ l_{fit} = 0.35t + \bar{l}_0 \]

(here \( \Delta f = 0.05 \) nN)
Force controlled simulations:

\[ \Delta f = \xi_f(f) \bar{v} \]
Force controlled simulations:

\[ \Delta f = \xi_f(f) \bar{v} \]

- \( f_0 = 1.00 \text{ nN} \): \( \Delta f = 0.0016 \bar{v} \)
- \( f_0 = 0.67 \text{ nN} \): \( \Delta f = 0.0013 \bar{v} \)
- \( f_0 = 0.33 \text{ nN} \): \( \Delta f = 0.0009 \bar{v} \)
Our next aim is to determine the length controlled rate law:

$$\Delta \bar{\bar{f}} = \xi_l(l)v.$$  \hspace{1cm} (17)

The samples are equilibrated for 5 ns at a fixed length before the length is increased at a constant velocity.
Our next aim is to determine the length controlled rate law:

\[ \Delta \bar{f} = \xi_l(l)v. \] (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 \( l_0 = 52 \text{ Å} \) when we stretch the molecule at a constant velocity \( v = 4 \text{ m/s} \) from \( t = 0 \).
length controlled simulations:

\[ \Delta \bar{f} = \xi_l(l) v \]
length controlled simulations:

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

\[ \bar{f} = 0.21 \]

\[ f_{\text{fit}}(t) = 0.0035t + 0.22 \]
length controlled simulations:

\[ \Delta \bar{f} = \xi_l(l)v \]
length controlled simulations:

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

Figure: The estimated \( \Delta \bar{f} \) associated with stretching molecules of length \( l_0 = 52 \text{
Å} \) for stretching velocities \( 2 \text{--} 14 \text{ m/s} \), shown with a fitting curve from linear regression. All data points are averaged over 200 samples.

\[ f_{\text{fit}}(v) = 0.0014t - 0.013 \]
Friction coefficients

Length controlled
Force controlled

\[ \xi \text{ (10^{-12} kg/s)} \]

\[ l, \bar{l} \text{ (Å)} \]
Entropy production at $v = 14 \text{ m/s}$

Length controlled
Force controlled

$\xi (10^{-12} \text{ kg/s})$ vs $l, \bar{l} (\text{Å})$
Conclusion

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

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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.\(^6\)

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Conclusion

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