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Determining the Gaussian curvature modulus of lipid membranes in simulations:

A comparative study via global shape transformations and local stress distributions

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- Helfrich Curvature Elastic Theory
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The Gaussian Bending Modulus $\overline{\kappa}$

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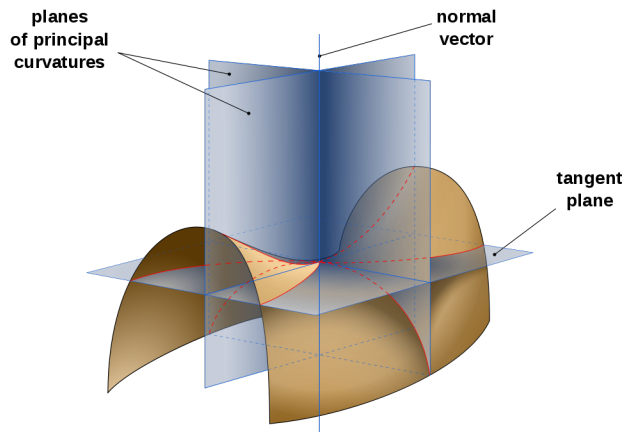
Helfrich theory [1] of membrane a patch $\mathcal{P}$

$$E[\mathcal{P}] = \int_{\mathcal{P}} \mathrm{d}A \left\{ \frac{1}{2}\kappa(K - K_0)^2 + \overline{\kappa} K_{\mathrm{G}} \right\} + \oint_{\partial\mathcal{P}} \mathrm{d}s\, \gamma \,.$$

- K total curvature ($K = c_1 + c_2$)
- K_{G} Gaussian curvature ($K_{\mathrm{G}} = c_1 \cdot c_2$)
- K_0 spontaneous curvature
- κ bending modulus
- γ line tension
- $\overline{\kappa}$ Gaussian bending modulus



Courtesy to Wikipedia.

[1] Helfrich, W., *Phys. Lett. A.* **50**, 115-116 (1973); Fromherz, P., *Chem. Phys. Lett.* **94**, 259-266 (1983)

Special Remarks on $\overline{\kappa}$

Why important and why hard to measure

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According to the Gauss-Bonnet theorem,

$$\int \mathrm{d}A\ K_{\mathrm{G}} = 4\pi(1-g) + \int \mathrm{d}s\ k_{\mathrm{g}}$$

the Gaussian term depends only on the *topology* and the *boundary*, which means:

- If both of them stay unchanged, then the K_{G} term is strictly irrelevant.
- In case that $\Delta \mathrm{g} = 1$, $|\Delta E| = 4\pi\overline{\kappa} \simeq 200 k_{\mathrm{B}} T$.
- Now if one wants to measure $\overline{\kappa}$, processes that control over topology and/or boundary are necessary.

Existing Measurements on $\overline{\kappa}$

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system	$-\overline{\kappa}/\kappa$	layer
egg lecithin	0.83 ± 0.12	bi
DOPE-Me	0.83 ± 0.08	mono
DOPE-Me	0.90 ± 0.09	mono
DOPE	0.92 ± 0.11	mono
DOPC	0.84 ± 0.17	mono
DOPC/Chol (1:1)	0.76 ± 0.10	mono
GMO/DOPC/DOPE	0.75 ± 0.08	mono
DOPC:SM:Chol	0.9 ± 0.38	bi
DOPC:SM:Chol	$0.31 \ldots 0.63$	bi

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Patch-closure Process and $\overline{\kappa}$

Main Idea

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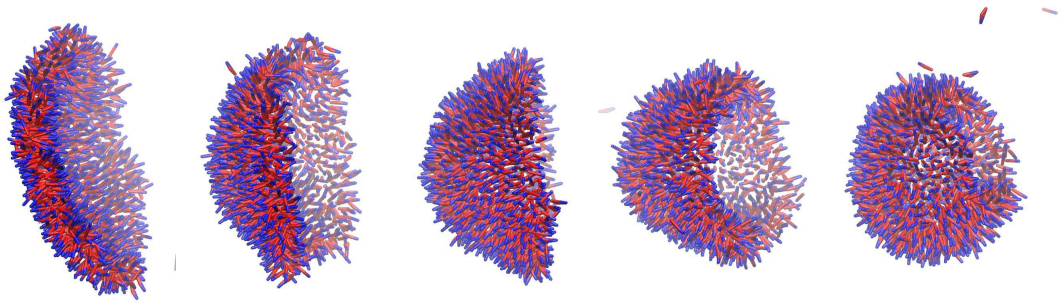
Helfrich theory of membrane elasticity

$$E[\mathcal{P}] = \int_{\mathcal{P}} \mathrm{d}A \left\{ \frac{1}{2}\kappa(K - K_0)^2 + \overline{\kappa} K_{\mathrm{G}} \right\} + \oint_{\partial\mathcal{P}} \mathrm{d}s\, \gamma \,.$$

Study the vesiculation process of a patch of membrane. [2]



$$\overline{\kappa} \Leftrightarrow \text{Critical Shape}$$

[2] Helfrich, W., *Phys. Lett. A.* **50**, 115-116 (1973); Fromherz, P., *Chem. Phys. Lett.* **94**, 259-266 (1983)

Patch-closure Process and $\overline{\kappa}$

Theory

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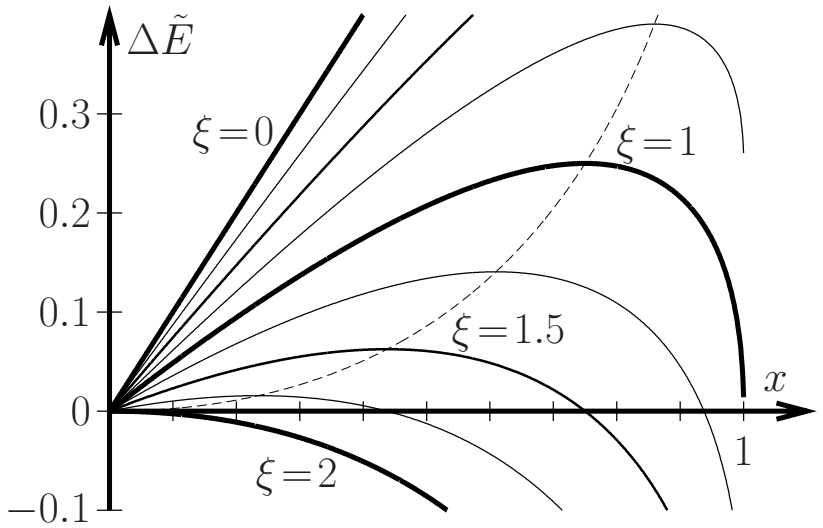
Assuming the patch stays as part of a sphere, the *excess* energy ΔE of a curved patch of area A is given by[3]

$$\Delta\tilde{E}(x,\xi) = \frac{\Delta E(x,\xi)}{4\pi(2\kappa+\overline{\kappa})} = x + \xi\left[\sqrt{1-x}-1\right] ,$$

where

$$R = \sqrt{\frac{A}{4\pi}}, x = (Rc)^2, \xi = \frac{\gamma R}{2\kappa+\overline{\kappa}} .$$



Instead of simulating a barrier-crossing problem, we prepare the system at specific x's and let it evolve *"like a rolling stone"*.

[3] Hu, M. *et al.*, *Biophys. J.* **102**, 1403 (2012)

Patch-closure Process and $\overline{\kappa}$

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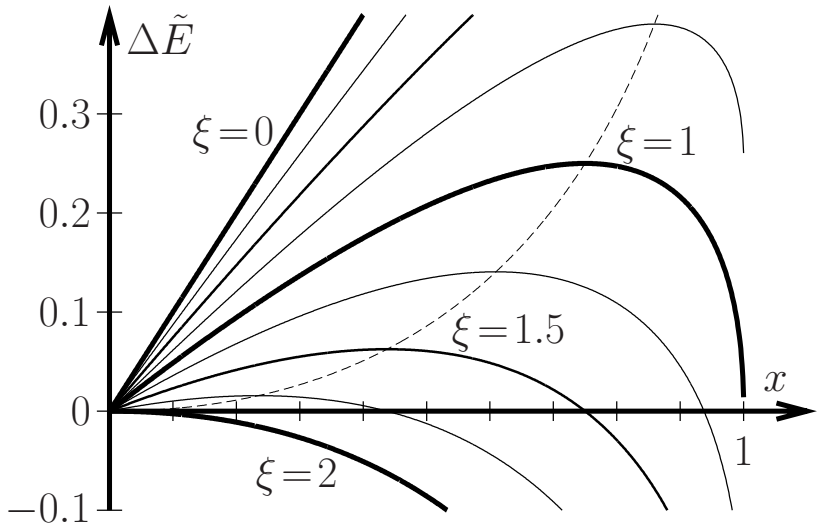

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Patch-closure Process and $\overline{\kappa}$

Probability of Patch Closure - Example Result

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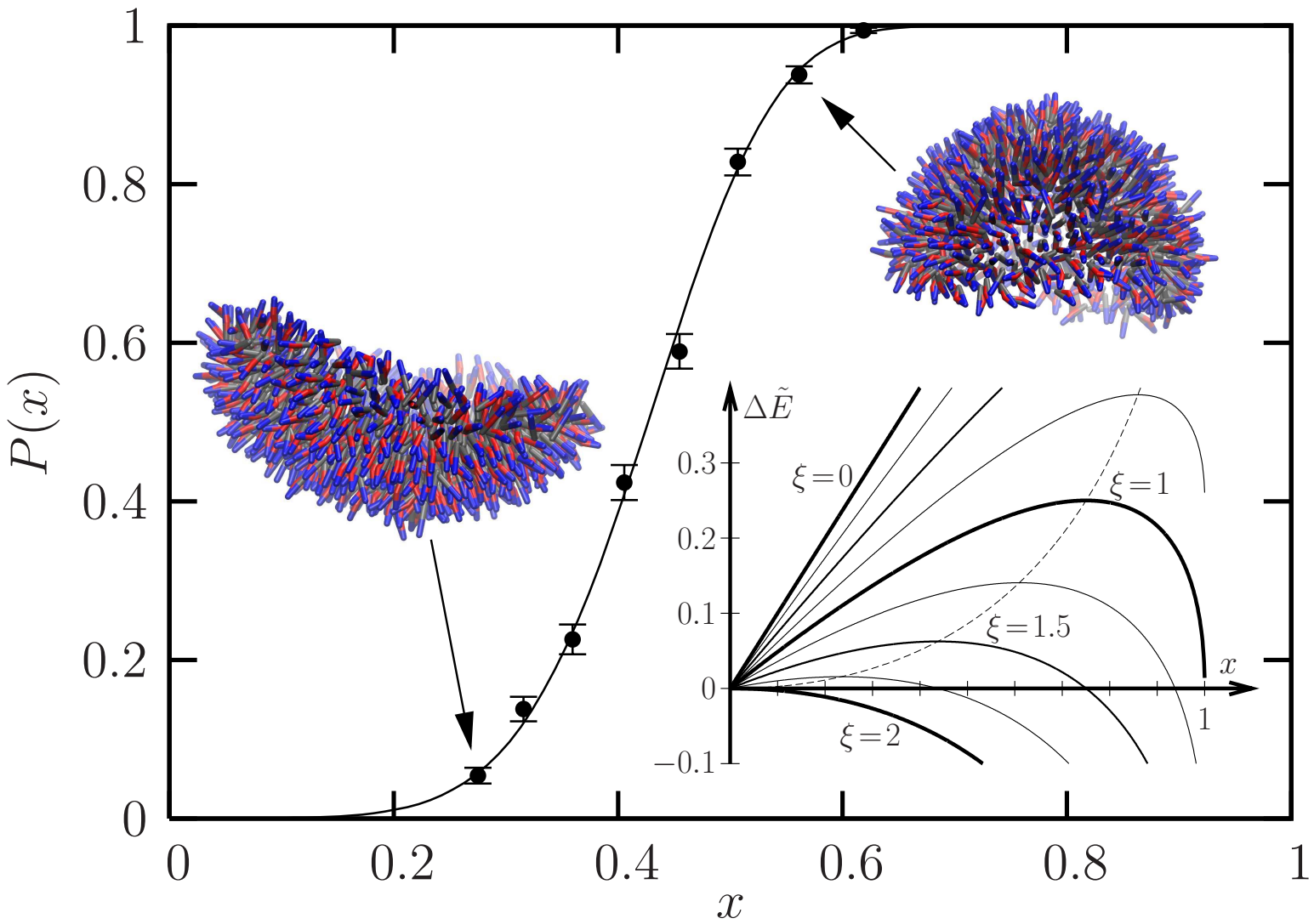

Patch-closure Process and $\overline{\kappa}$

Constraining Forces *in Equilibrium*

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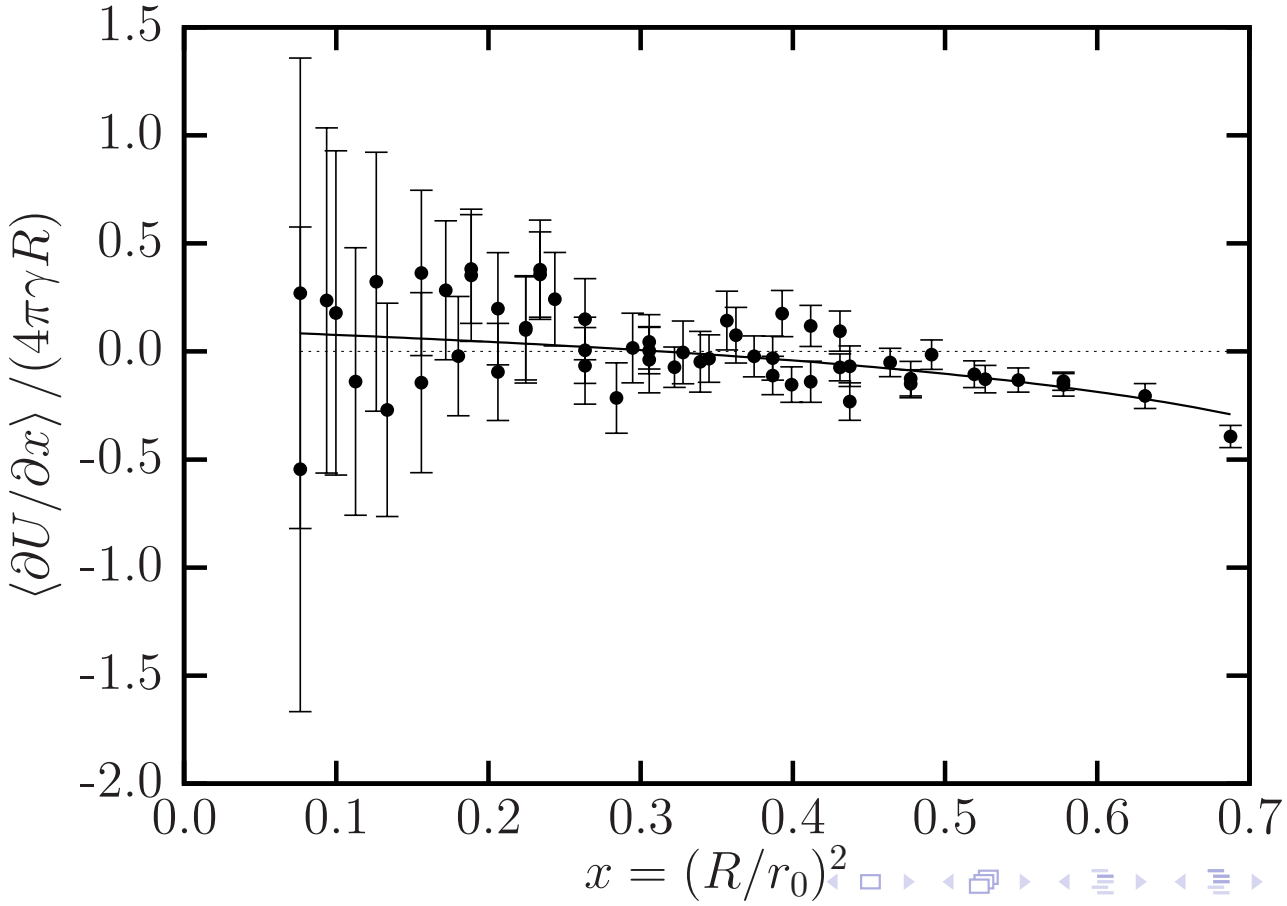
$$\Delta E(x) = \int_0^x \mathrm{d}y \left\langle \frac{\partial U(y)}{\partial y} \right\rangle , \quad \frac{1}{4\pi\gamma R} \left\langle \frac{\partial U(x)}{\partial x} \right\rangle = \frac{1}{\xi} - \frac{1}{2\sqrt{1-x}} .$$



Patch-closure Process and $\overline{\kappa}$

Results

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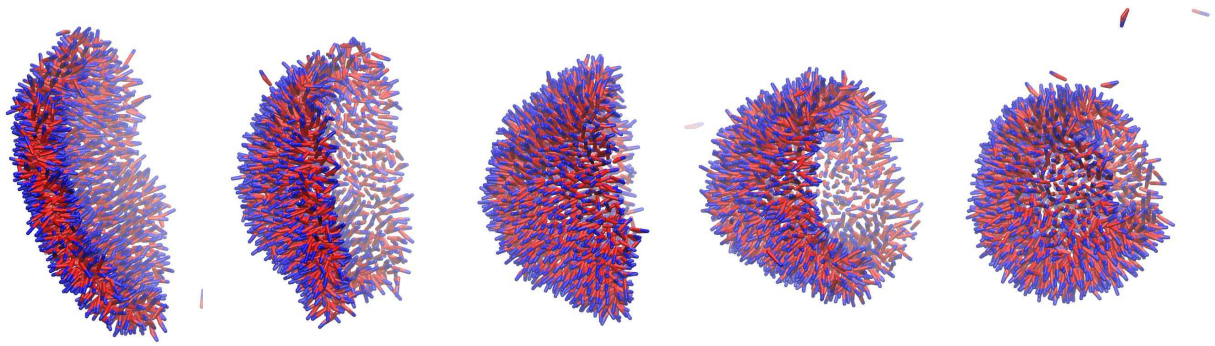

$w_c\,[\sigma]$	N_{lipid}	ξ	$\overline{\kappa}/\kappa$ †	$\overline{\kappa}/\kappa$ ‡
1.6	900	1.606 ± 0.089	-0.93 ± 0.03	-1.00 ± 0.06
1.6	1000	1.676 ± 0.053	-0.92 ± 0.03	-0.99 ± 0.04
1.6	1100	1.633 ± 0.111	-0.91 ± 0.03	-0.92 ± 0.08
1.7	900	1.423 ± 0.029	-0.90 ± 0.02	-0.89 ± 0.03
1.7	1000	1.434 ± 0.060	-0.87 ± 0.02	-0.84 ± 0.05
1.7	1100	1.522 ± 0.059	-0.86 ± 0.02	-0.85 ± 0.05

† Results using the probabilistic patch-closure method.
‡ Results using the equilibrium method;

Stress Profile Method

Theory Summary

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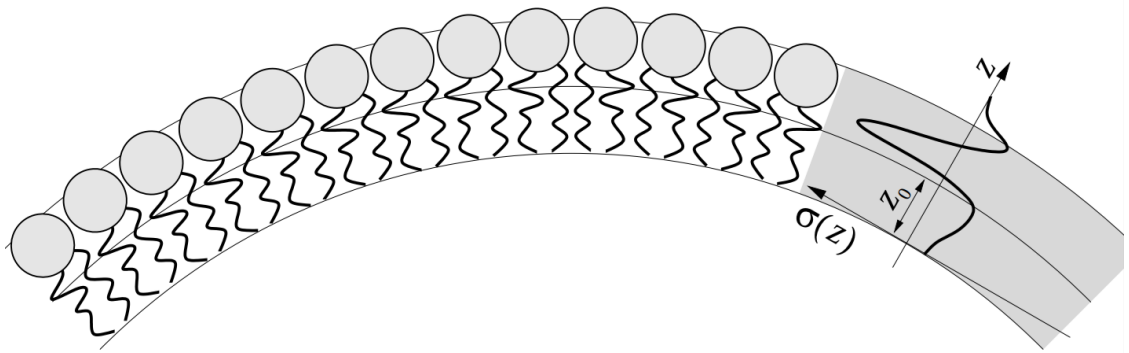

The lateral stress profile of a *flat* and *tension-free* membrane can be related to its elastic properties as [4]

$$\overline{\kappa} = \int_{-\infty}^{\infty} \mathrm{d}z\, z^2\, \Sigma_0(z)\ ,$$

$$-\kappa_{\mathrm{m}} K_{0\mathrm{m}} = \int_{0}^{\infty} \mathrm{d}z\, (z - z_0)\, \Sigma_0(z)\ ,$$

$$\overline{\kappa}_{\mathrm{m}} = \int_{0}^{\infty} \mathrm{d}z\, (z - z_0)^2\, \Sigma_0(z)\ .$$

[4] Helfrich, W. In *Physics of Defects*;

Stress Profile Method

Example Result

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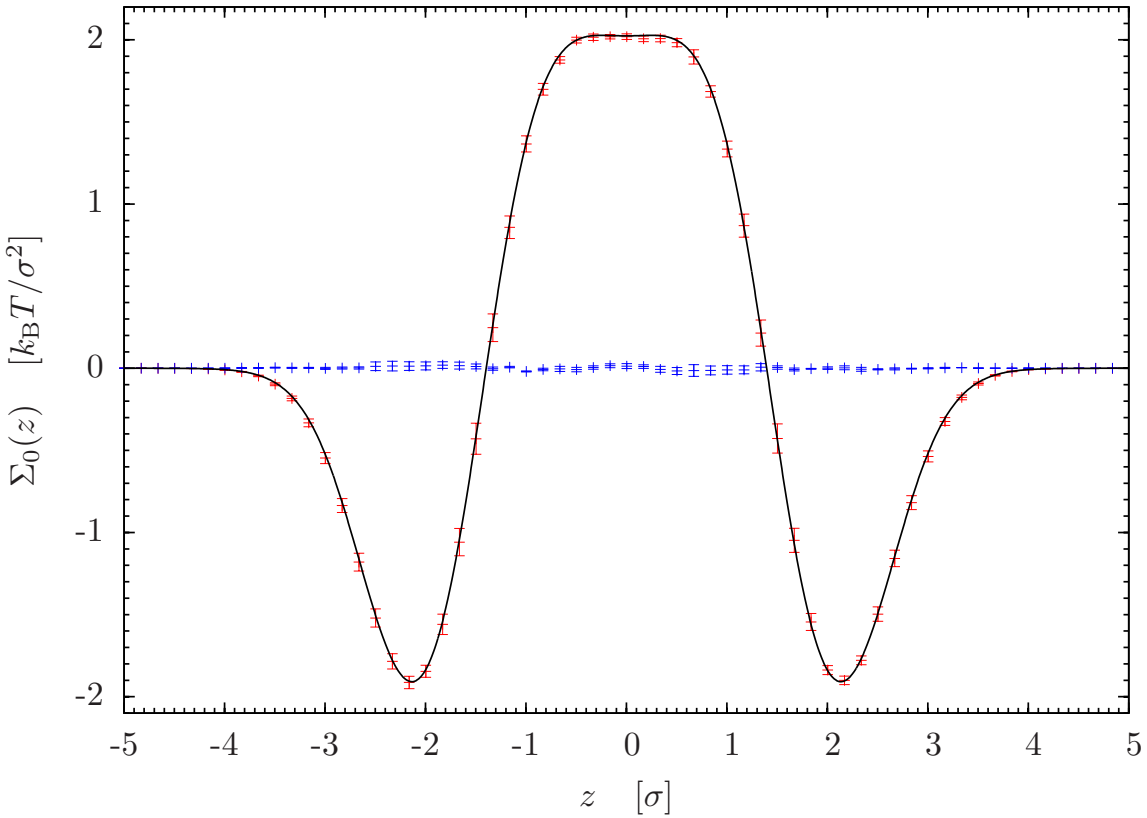

$$\overline{\kappa}/\kappa \simeq -1.7$$

$$\frac{\overline{\kappa}_m}{\kappa_m} \simeq -0.9 \quad \Rightarrow \quad z_0 \simeq 0.7\,\sigma$$

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MARTINI model[5]

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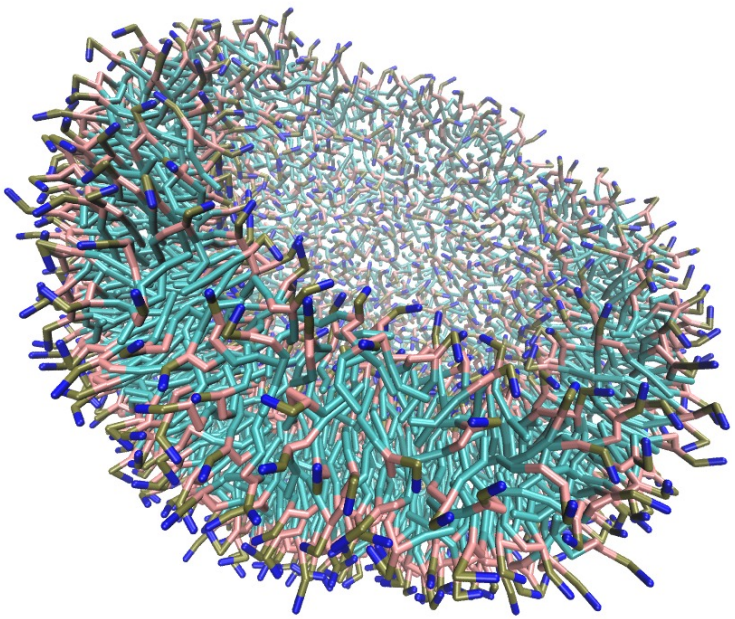

γ [pN]	ξ	κ [10^{-20}J]	$\overline{\kappa}$ [10^{-20}J]	$\overline{\kappa}/\kappa$
40.49 ± 0.34	1.359 ± 0.004	16.6 ± 0.5	-17.3 ± 1.0	-1.04 ± 0.03

Faraday Discussion 161 accepted. DOI: 10.1039/C2FD20087B

[5] Marrink, S.J. *et al.*, *J. Phys. Chem. B.* **111**, 7812 (2007)

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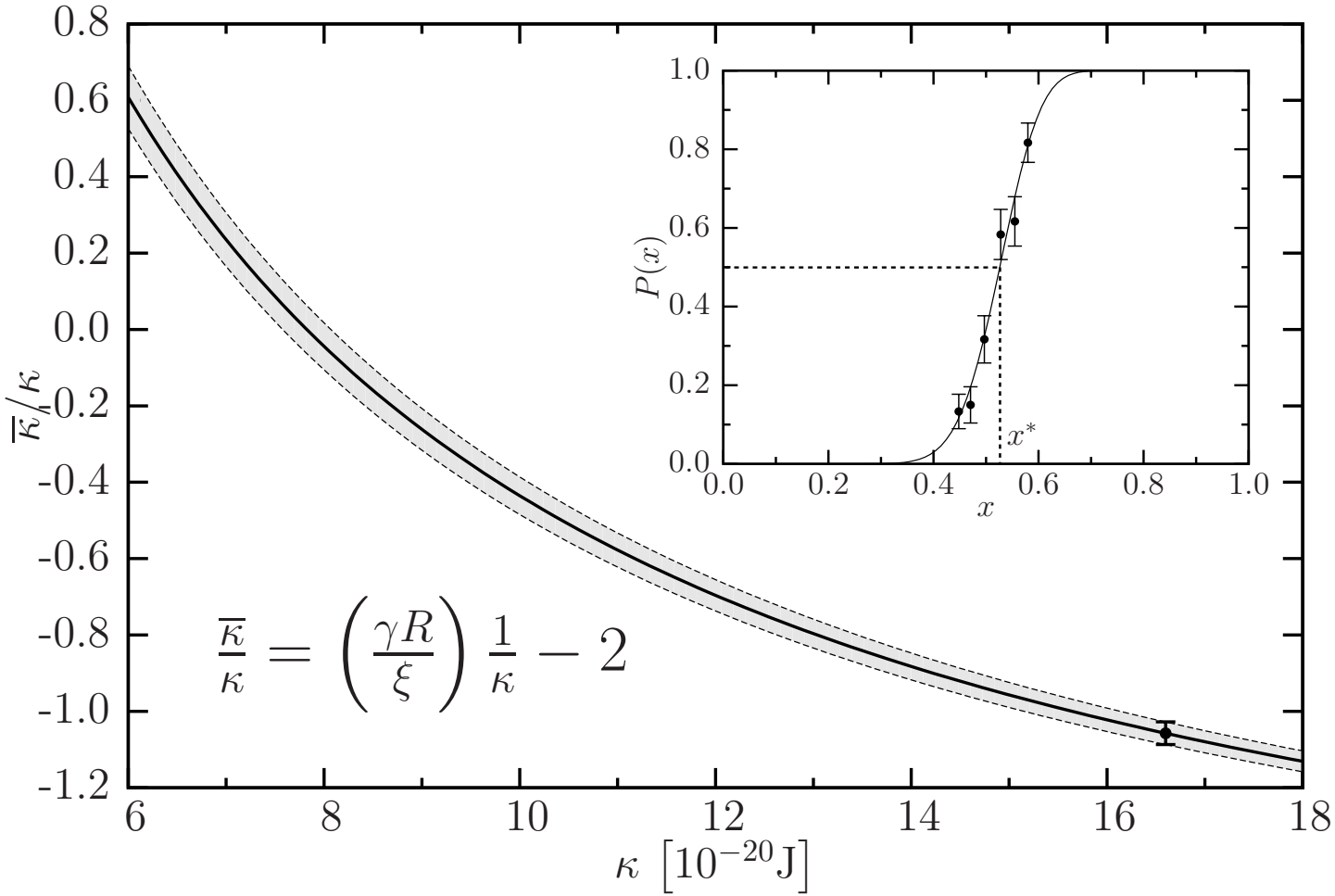

Make sure parameters are *self-consistent*!

MARTINI model

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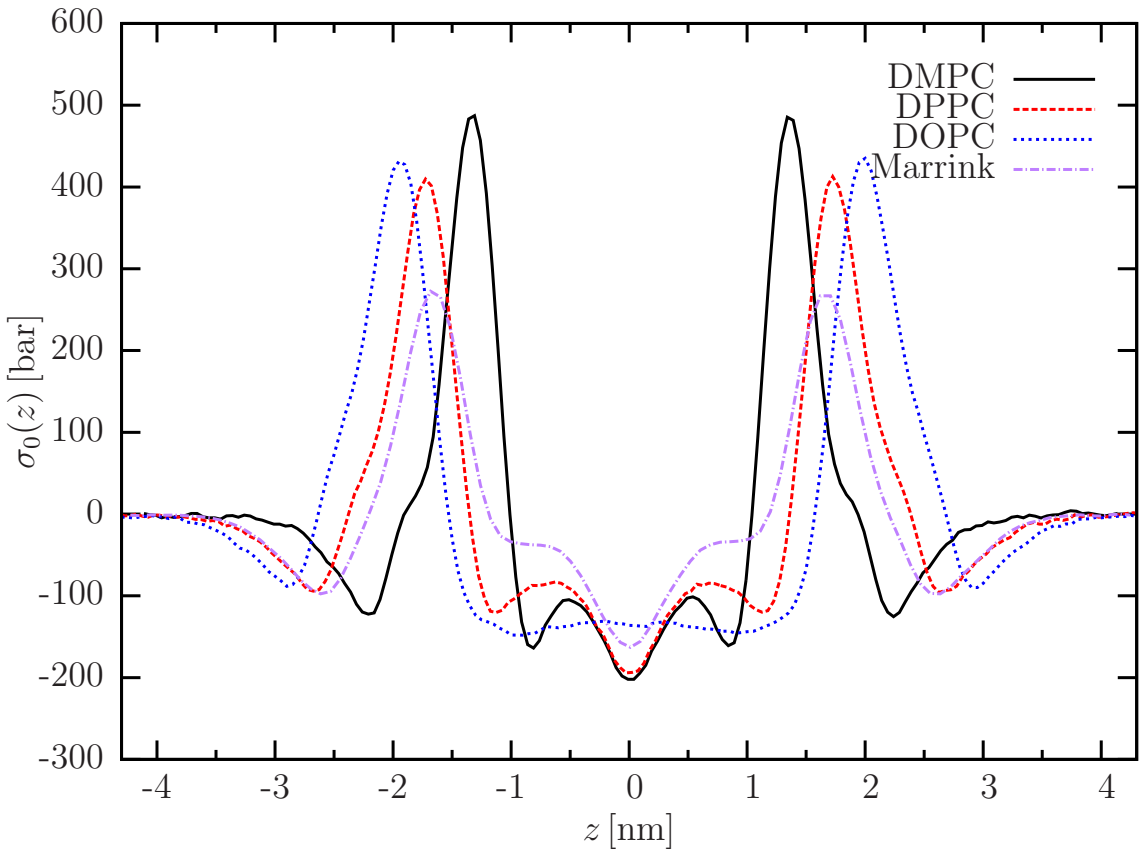

Lipid	$N_L \mid \frac{4N_W}{N_L}$	T [K]	Σ [$\frac{mN}{m}$]	K_{0m} [nm^{-1}]	$\overline{\kappa}/\kappa$
DMPC	256|46	300	0.09 ± 0.08	-0.070 ± 0.001	-0.053 ± 0.003
DPPC	256|42	323	0.12 ± 0.08	-0.146 ± 0.001	0.135 ± 0.004
DOPC	256|41	300	0.14 ± 0.08	-0.246 ± 0.001	0.481 ± 0.004

Thank you!

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