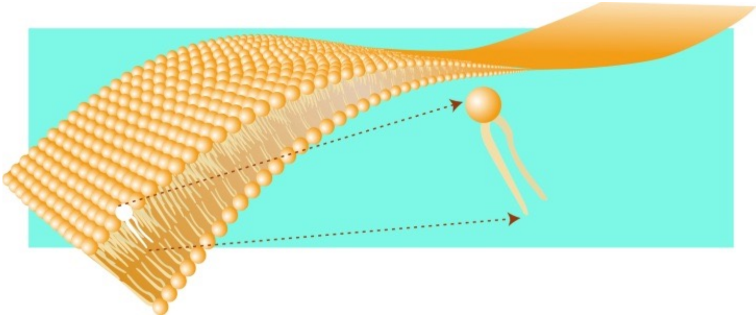
Membrane viscosity effects on dynamics of fluid bilayers

Petia M. Vlahovska
Engineering Sciences and Applied Mathematics
Northwestern University, Evanston, USA

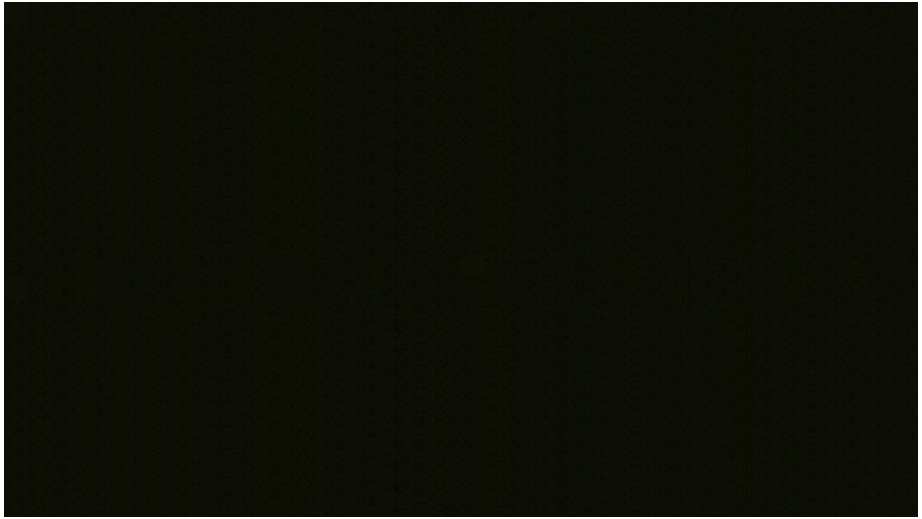
Rumiana Dimova (MPIKG, Germany)
Rony Granek (BGU, Israel)
Hammad Faizi (NWU, USA)

Biomembranes

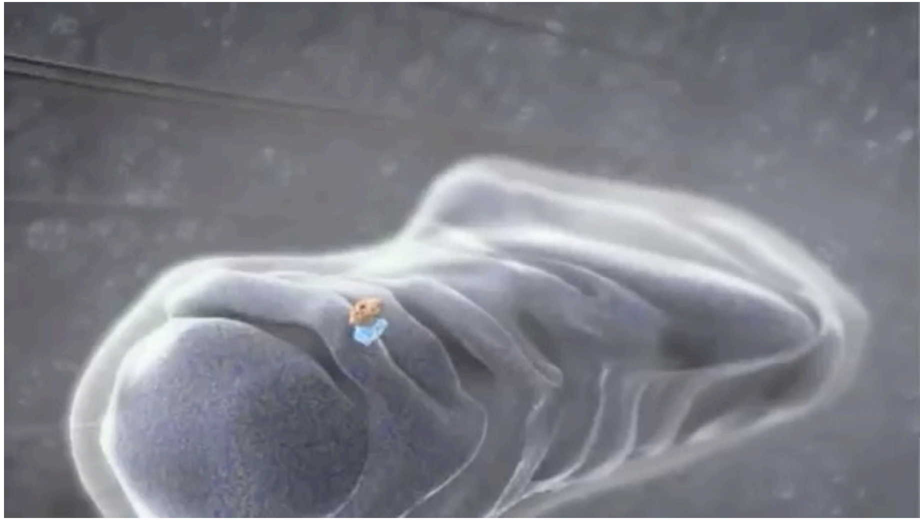


Cells and cellular organelles are enveloped by membranes, whose main structural component is a lipid bilayer.

Membranes are fluid



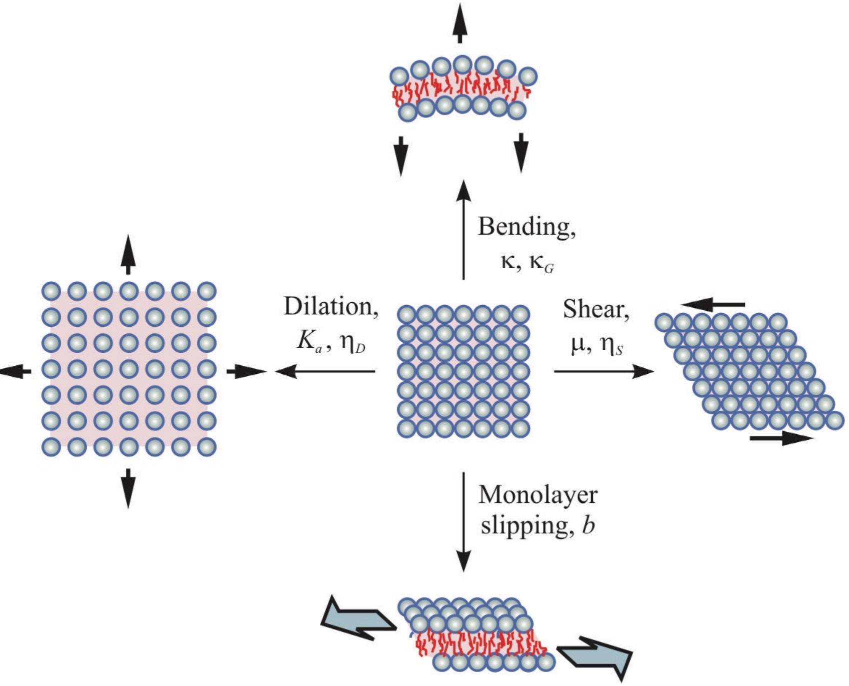
Membranes are constantly deformed



From the "Inner Life of the Cell"

Lipid bilayers: solid-fluid duality

modes of deformation



Dimova et al. J. Phys. Cond. Mat. (2006)

Bending (Helfrich)

$$E = \int dS \left(2\kappa H^2 + \kappa_G K\right)$$

Dissipation (incompressible 2D Newtonian fluid)

$$P_s = \int dS \left(\eta_s \mathbf{d} : \mathbf{d}\right)$$

Boussinesq–Scriven model

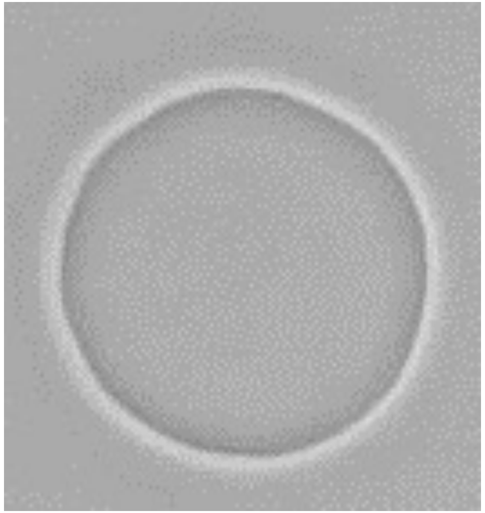
$$\mathbf{d} = \frac{1}{2}\left(\nabla_s \mathbf{v} + \nabla_s \mathbf{v}^T\right) + v_n \nabla_s \mathbf{n}$$

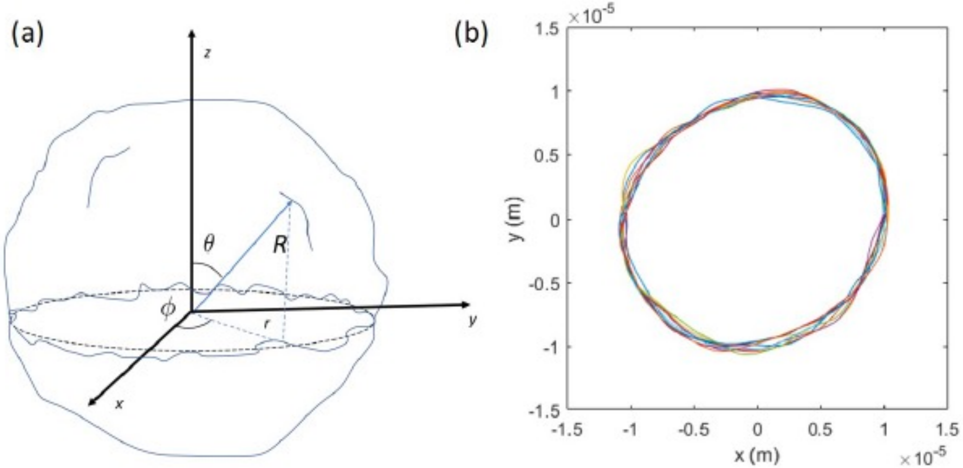
$$P_b = \int dS \frac{b}{2}\left(\mathbf{v}^+ - \mathbf{v}^-\right)^2$$

Rahimi et al. Soft Matter (2013)
Fournier Int. J. Non-lin. Mech. (2015)

How to measure the membrane mechanical properties?

Lipid bilayers are soft: membrane fluctuations





Thermally driven shape fluctuations of a giant unilamellar vesicle (GUV) (radius ~20microns)

A typical value of the bending rigidity of a lipid bilayer is $\kappa \sim 20 k_B T$

Faizi et al, Soft Matter (2020)

Lipid bilayers are soft: membrane fluctuations

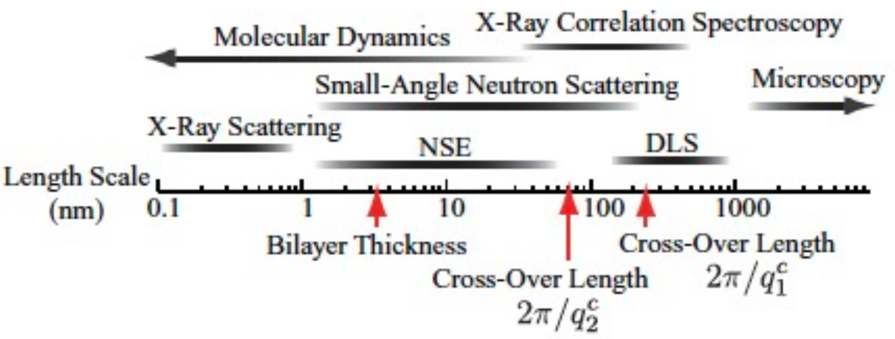


FIG. 1. Membrane fluctuations have been studied across several length scales using a wide variety of techniques. The ranges of applicability for several techniques are shown above. Using the constants from Fig. 5, we also show the bilayer thickness and cross-over wavelengths $q_{1,2}^c$ associated with DMPC (see Sec. II).

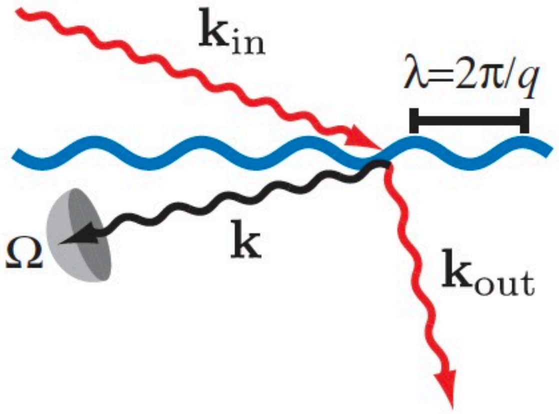


FIG. 6. The scattering wave vector $\mathbf{k}$ is defined as the difference between the incident and outgoing wave vectors $\mathbf{k} \equiv \mathbf{k}_{out} - \mathbf{k}_{in}$. In order to calculate $S(k, t)$, we integrate $S(\mathbf{k}, t)$ over all solid angles Ω. The membrane (blue) is shown with wavenumber $q = 2\pi/\lambda$.

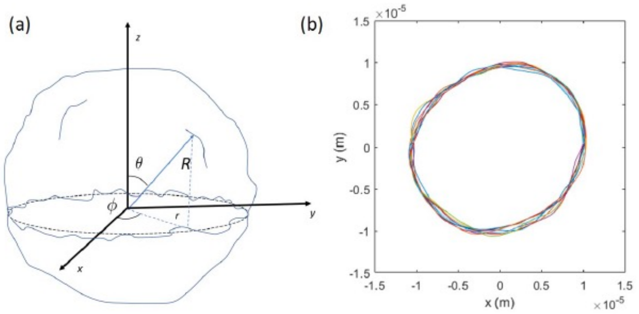
Watson and Brown, J. Chem. Phys. (2011)

intermediate scattering function

$$S(k,t)/S(k,0) \sim e^{-(\Gamma(k)t)^{2/3}}$$

Analysis of the decay rate Γ yields the bending rigidity κ

Theoretical models for S(q,t)   planar membrane $\Leftrightarrow$ wavelength $\ll$ vesicle radius



Vesicle contour in the equatorial plane

$$r(\phi,t) = R_0 \sum u_q(t) q^{-iq\phi}$$

simplest model: 2D incompressible ``Helfrich" interface

$$\langle |u_q|^2 \rangle = \frac{k_B T}{\kappa q^4 + \sigma q^2}$$

η: bulk viscosity
κ: bending rigidity
σ: tension

$$\langle u_q(0) u_q^*(t) \rangle = \langle |u_q|^2 \rangle e^{-t/\tau_q} \qquad t_q = \frac{4\eta}{\kappa q^3 + \sigma q}$$

$$S(k,t) \sim S(k) e^{-(\Gamma_{ZG}(k)t)^{2/3}} \quad \mathrm{t} \ll t^* \qquad \Gamma_{ZG}(k) = 0.025\gamma \frac{(k_B T)^{3/2}}{\kappa^{1/2}\eta} k^3$$

Membrane viscosity does not affect time correlations/dynamics!

Brochard and Lennon, J. Phys. (1975)
Zilman and Granek, PRL (1996)

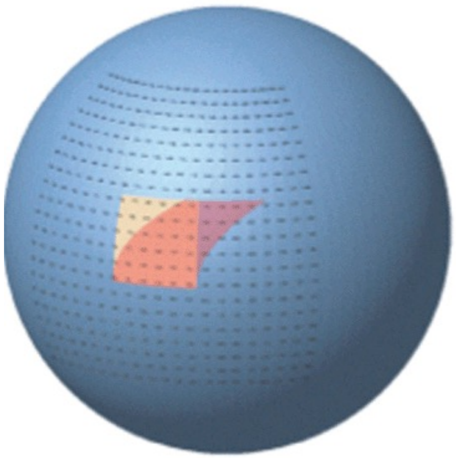
Modeling the bilayer as slightly compressible membrane composed of two coupled monolayers:
Seifert-Langer Europhys. Lett. (1993)
Watson and Brown, Biophys. J. (2010), J. Chem. Phys. (2011))

$$\kappa \to \tilde{\kappa} = \kappa + 2k_m d^2$$

But vesicles are quasi-spherical: shouldn't curvature matter?

wavelength ~ radius $\Longrightarrow$ spherical membrane

intrinsic curvature results in shearing of the transported material, since neighboring fluid elements travel paths of different lengths



Sigurdsson and Atzberger, Soft Matter (2016)

Watson and Brown, J. Chem. Phys. (2011) discuss the potential implication of geometry on S(q,t)

Henle et al. EPL (2008)
Henle and Levine, PRE (2010)
Honnercamp et al., PRL (2013)
Rahimi et al, Soft Matter (2013)
Sigurdsson and Atzberger, Soft Matter (2016)
Al-Izzi and Morris, arXiv:2103.12264 (2021)

Fluctuations: Rochal et al PRE (2005)
Vesicle shape evolution with membrane viscosity (but no bilayer slip): Olla, Physica A (2000)

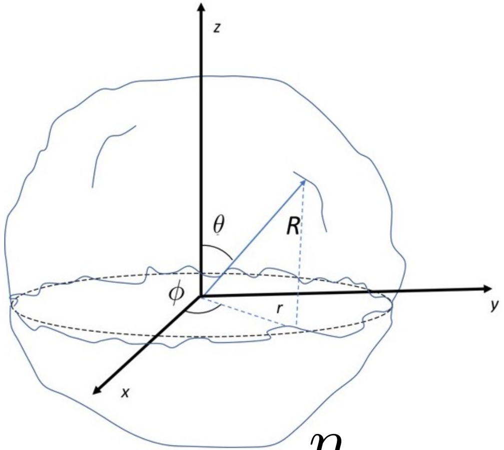
Shape fluctuations of a quasi-spherical viscous vesicle: revisited

$$R(\theta,\phi,t) = R_0\left(1 + \sum_{l=0}^{l_{max}} \sum_{m=-l}^{l} f_{lm}(t)\mathcal{Y}_{lm}(\theta,\phi)\right)$$

Dynamics including surface shear viscosity

$$\partial_t f_{lm} = -\omega_l f_{lm} + \zeta_{lm}(t)$$

$$\omega_l = \frac{\kappa}{R_0^3}\frac{l(l+1)(l+2)(l-1)\left(l(l+1)+\bar{\sigma}\right)}{4l^3+6l^2-1+4(-2+l+l^2)\lambda_m}$$



$$\lambda_m = \frac{\eta_m}{\eta R_0}$$

Fluctuations of a quasi-spherical vesicle: Safran-Milner, PRA (1996), Seifert EPJE (1999)
Fluctuations of a quasi-spherical vesicle including bilayer slip: Miao et al. EPJE (2002)
Fluctuations of a viscoelastic vesicle: Rochal et al PRE (2005)
Vesicle shape evolution with membrane viscosity: Olla, Physica A (2000)

Vlahovska, Chapter 9 in Fluid–Structure Interactions in Low-Reynolds-Number Flows (2016)
Vlahovska and Misbah, Chapter 7 in "The Giant Vesicle Book" (2020)

Vesicle fluctuations with bilayer slip and membrane viscosity: coming!

Modified relaxation rate:

$$\omega_l = \frac{\kappa}{R_0^3 \eta} \frac{l(l+1)(l+2)(l-1)\left(l(l+1)+\bar{\sigma}\right)}{(4l^3+6l^2-1)+4(-2+l+l^2)\lambda_m}$$

Planar membrane result: $\lambda_m = 0\,, \quad l \gg 1 \quad \omega_l \sim \dfrac{\kappa}{4R_0^3\eta} l^3$

$$\lambda_m \gg 1 \quad \text{and} \quad l \ll \lambda_m \quad \omega_l \sim \frac{\kappa}{R_0^2 \eta_m} l^4$$

Crossover mode: $l^* = \lambda_m = \dfrac{\eta_m}{\eta R_0}$

modes with $l<l^*$ are affected, short wavelengths relax with rate controlled by dissipation in the bulk

Does it matter?

Consider lipid membrane viscosity 10^{-9} Pa.s.m, bulk (water) viscosity 10^{-3} Pa.s

GUVs: R_0=10 microns, λ_m=0.1 (negligible effect)

Liposome:
R_0=100nm, λ_m=10. All modes up to 10 will be affected.
R_0=50nm, λ_m=20. All modes up to 20 will be affected.

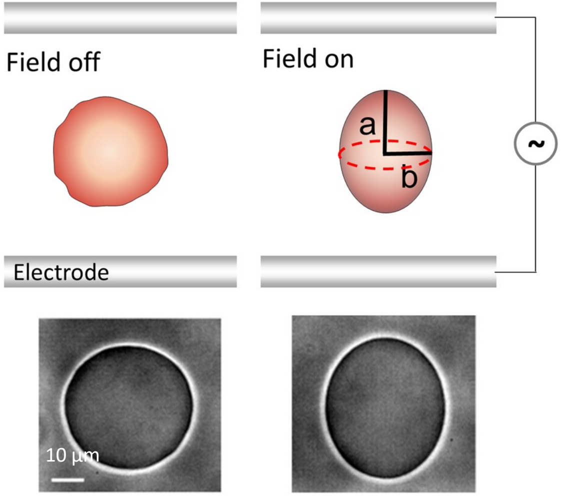
$$\lambda_m = \frac{\eta_m}{\eta R_0}$$

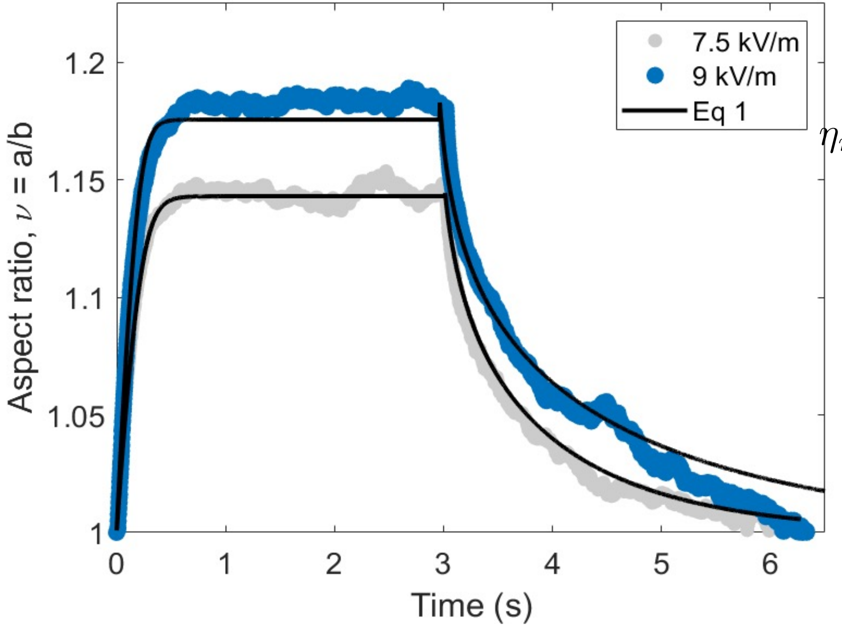
Saffman-Delbruck length compared to vesicle radius, < 1µm

If membrane viscosity 10^{-8} Pa.s.m:
GUVs: R_0=10 microns, λ_m=1 (still negligible effect)
Liposome: R_0=50nm, λ_m=200!

Can we detect the membrane viscosity effect in GUVs?

Excite only the l=2 mode (e.g., by applying extensional stress *p*)





POPC

$$\eta_m = 2 \times 10^{-7} N.s/m$$

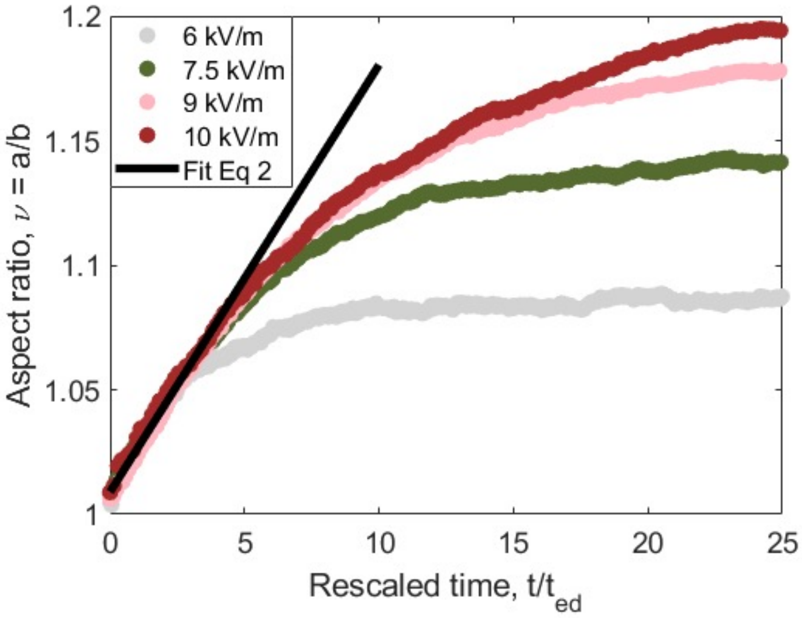
deformation/relaxation curve of the same vesicle at different E

$$\dot{\nu} = \frac{1}{\eta\left(55 + 16\lambda_m\right)}\left(p - \frac{24\sigma(\nu)}{R_0}(\nu - 1)\right)$$

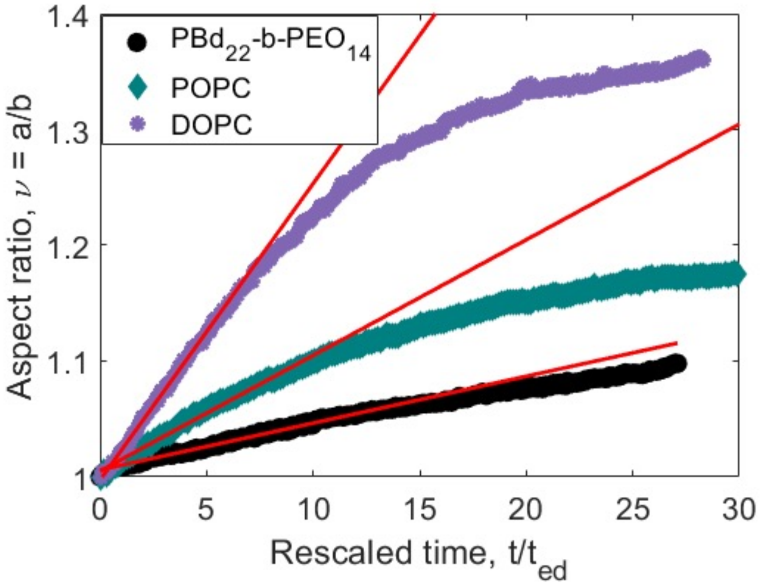
η: bulk viscosity
p: applied stress
σ: tension

Faizi et al. , arXiv:2103.02106

Initial deformation yields membrane viscosity



same vesicle at different E



different compositions

$$\nu = 1 + \frac{t}{t_d}\left(\frac{27}{8\,(55 + 16\lambda_m)}\right)$$

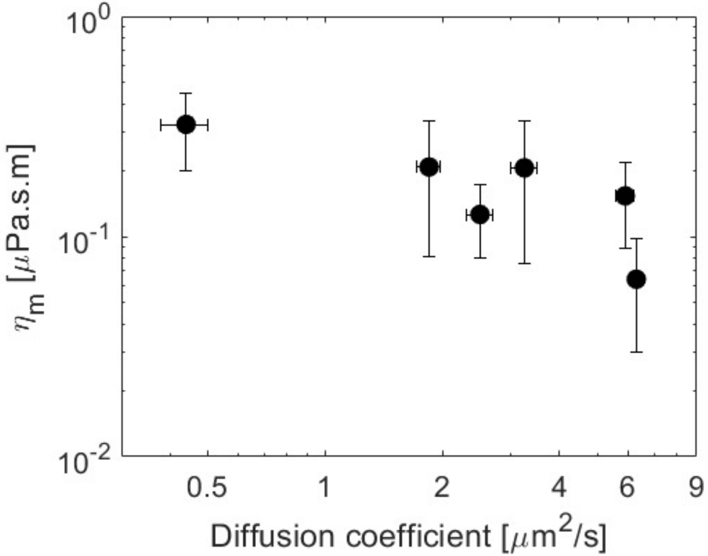
Faizi et al. , arXiv:2103.02106

Some results from the deformation method

Table 1. Apparent membrane viscosity of single-component bilayers at temperature 25.0°C. The values in brackets indicate tail unsaturation (first column) and the number of analyzed vesicles (last column).

Composition	η_m [10^{-8} Pa.s.m]
DOPC (18:1)	6.4 ±3.4 (19)
POPC (16:0-18:1)	23.4 ±11.1 (21)
SOPC (18:0-18:1)	21.4 ±4.0 (20)
DMPC (14:0)	48.0 ±15.8 (17)

reported values for DOPC: 0.197 ± 0.0069 x 10^{-9}Pa.s.m from MD simulations (Zgorski et al, JCTC, 2019), 1.9±11x10^{-9} Ps.s.m measured by domain tracking on giant vesicles (Honerkamp et al, PRL 2013) to 16.72±1.09x10^{-9} Pa.s.m measured by Neutron Spin Echo (Chakraborty et al, PNAS 2020)

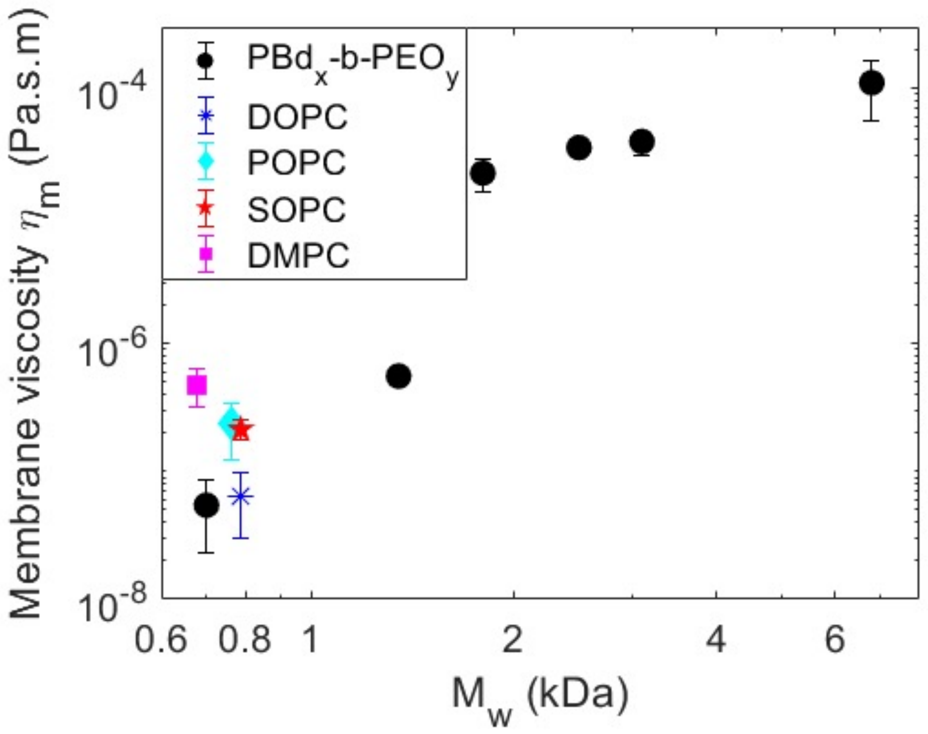


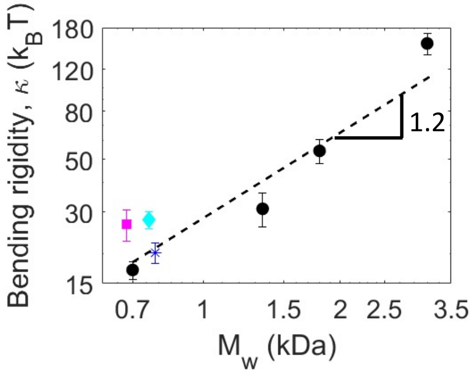
Membrane viscosity of DOPC/DPPC/Chol bilayers vs lipid diffusivity values obtained with FCS by Scherfeld et al. Biophys. J (2003)

Questions:

- Why membrane viscosity obtained from MD simulations is so much smaller than the value obtained by other methods?
- 2D viscosity vs diffusivity as a reporter for membrane fluidity?

Some results from the deformation method





Membrane thickness scales with molecular weight as

$$h \sim M_w^n \qquad n\text{=0.5-1}$$

If $\kappa \sim h^2 \implies \kappa \sim M_w^{2n}$

However, membrane viscosity does not show simple dependence on h

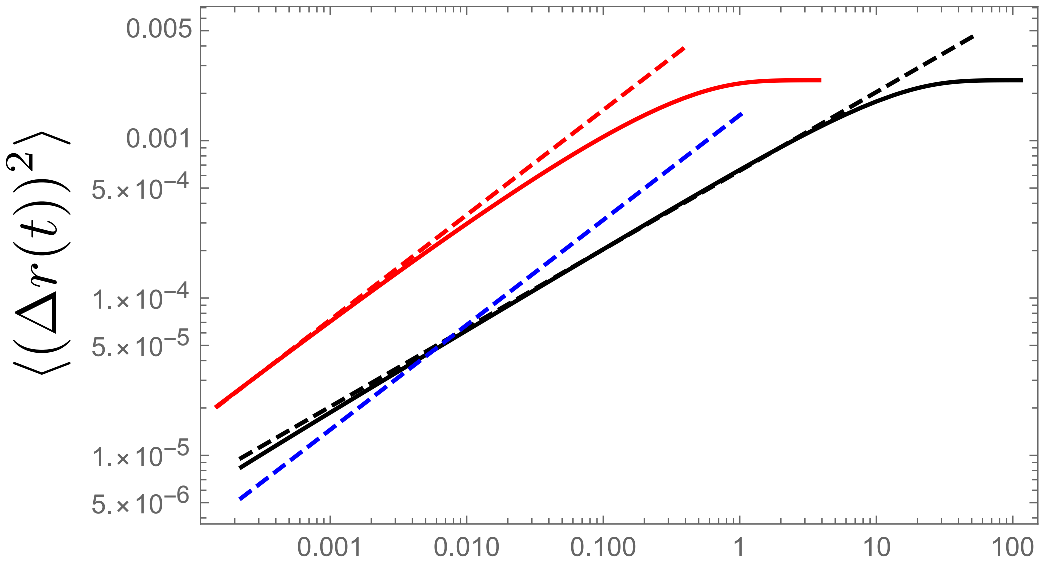
Questions:

- Does 2D viscosity really scale as $\eta_{2D} = \eta_{3D} h$?
- Could bilayers exhibit non-Newtonian rheology?

Coming back to fluctuations…

Membrane viscosity and dynamic structure factor

Let us consider the roughness $\langle(\Delta r(t))^2\rangle = \frac{1}{2\pi}\sum_{l=2}^{l_{max}}(2l+1)\langle f_{lm}^2\rangle\left(1-e^{-\omega_l t}\right)$



Time scaled by $t_\kappa = \frac{\eta R_0^3}{\kappa}$

The line is the full theory, and the dashed line is the asymptotic behavior for short times (R. Granek)

Red: λ_m=0

$\sim \kappa^{-1/3}t^{2/3}$

Black: λ_m=100

$\sim \kappa^{-1/2}\lambda_m^{-1/2}t^{1/2}$

Blue: λ_m=0

$\sim \kappa_{\text{eff}}^{-1/3}t^{2/3}$

$\kappa_{\text{eff}} = 5\kappa$

Question: Could increase in membrane viscosity be misinterpreted as increase of bending rigidity?

Conclusion:
Membrane viscosity affects the dynamics of non-planar membranes with intrinsic curvature.

Questions:

1. Are bilayers always Newtonian fluids?
2. Why membrane viscosity obtained from MD simulations is so much smaller than the value obtained by other methods?
3. Viscosity vs probe diffusivity as a reporter for membrane fluidity?
4. Do we need to rethink the interpretation of data from NSE with liposomes?