量子ビームでさぐるソフトマターの物性

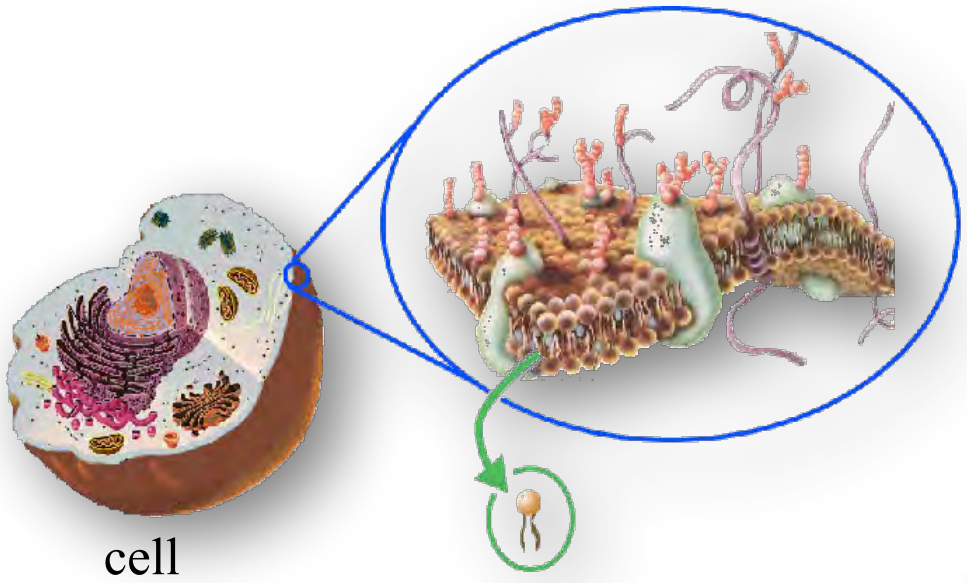
Water Dynamics

瀬戸秀紀

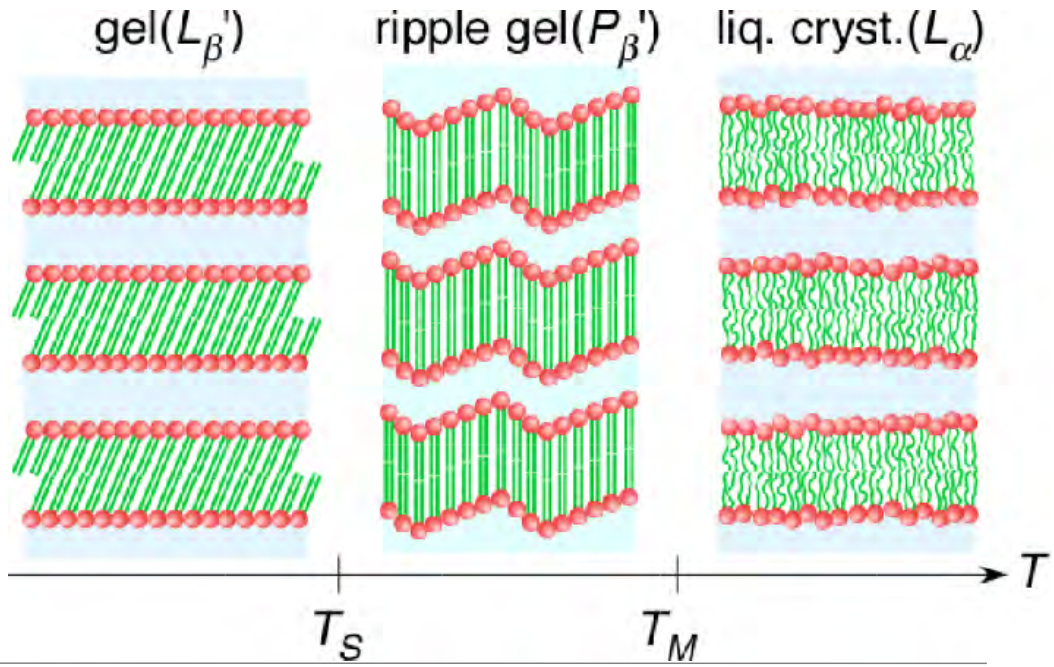
CROSS

High Energy Accelerator Research Organization

Phospholipids



bio membrane



Number of hydration water?

(THz spectroscopy)

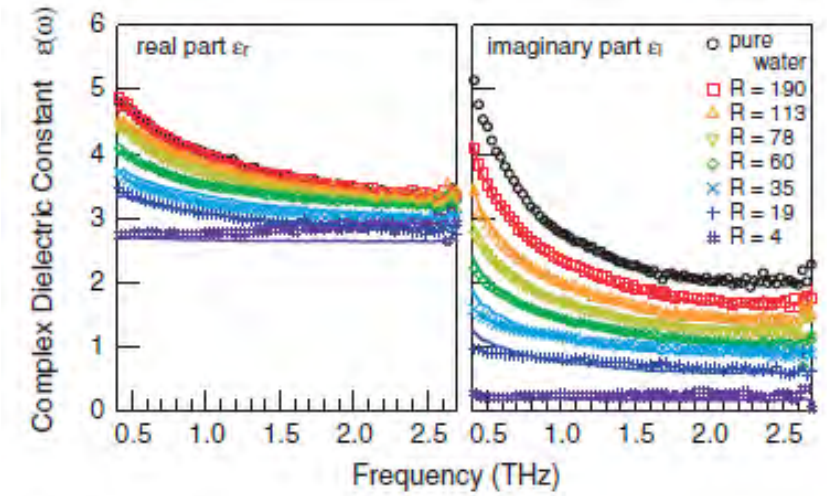


FIG. 2 (color). Complex dielectric constant of pure water, DMPC solutions ($R = 190, 113, 78, 60, 35, 19$), and DMPC film ($R = 4$), obtained by THz TDS measurements (0.4–2.7 THz). The left figure shows the real part of the dielectric constant, while the right one is the imaginary part. The solid lines show the fitting result by using Eq. (1) with fixing $r_h = 0.944$.

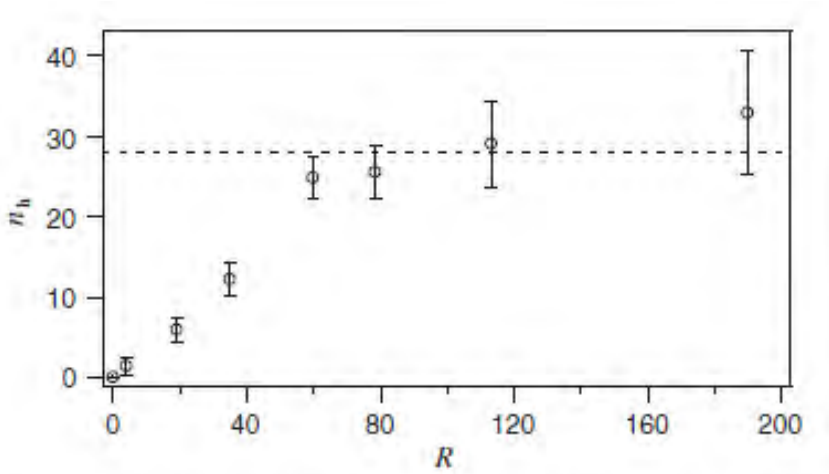


FIG. 3. Number of hydration water molecules per DMPC molecule, n_h, indicated in the 10^{-13} s scale. The results are obtained by using Eq. (1) with fixing $r_h = 0.944$ ($\sigma_w = 1.19$) and $\alpha_l = 86$ Å^3. The dashed line is at $n_h = 28.1$, i.e., the averaged value for the fully hydrated condition $R > 35$.

M. Hishida and K. Tanaka, *Phys. Rev. Lett.*, **106** (2011) 158102

Deuterated samples were used

T. Yamada, et al., *J. Phys. Chem.*, 2017

d_{67}DMPC-37H_2O

	Coherent scatt.	Incoherent scatt.
d_{67}DMPC	631.4 barn (8.5%)	631.4 barn (7.3%)
37H_2O	286.6 barn (3.9%)	5939.2 barn (80.3%)

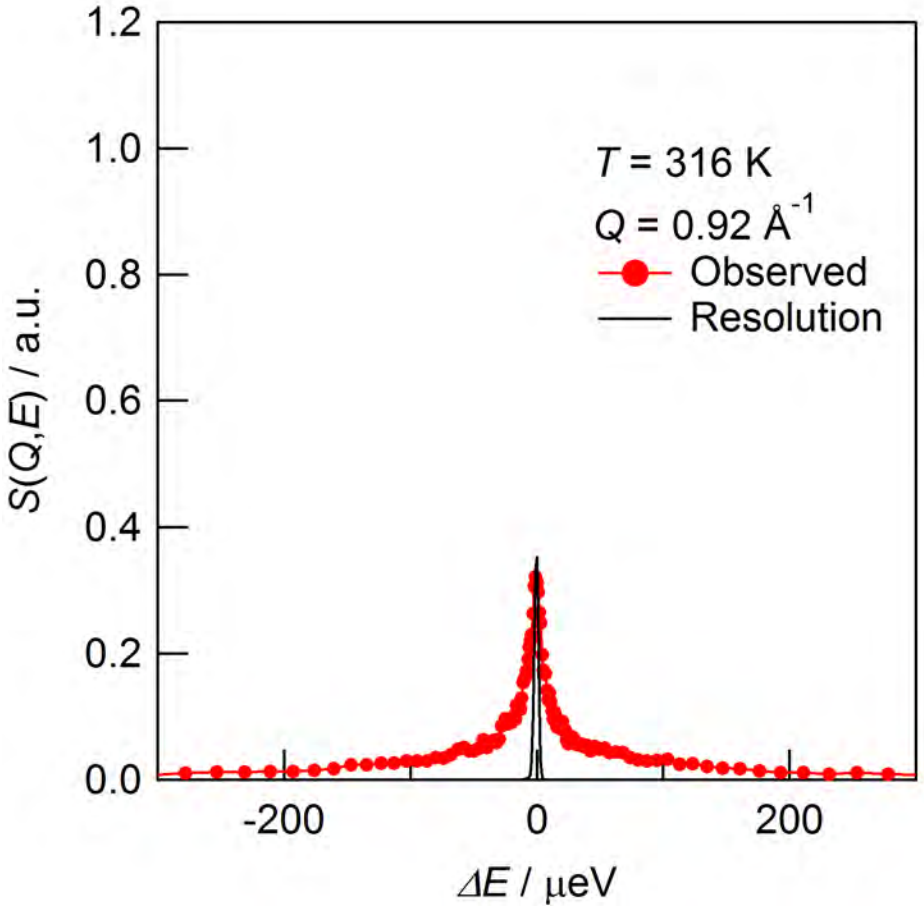
DMPC-35D_2O

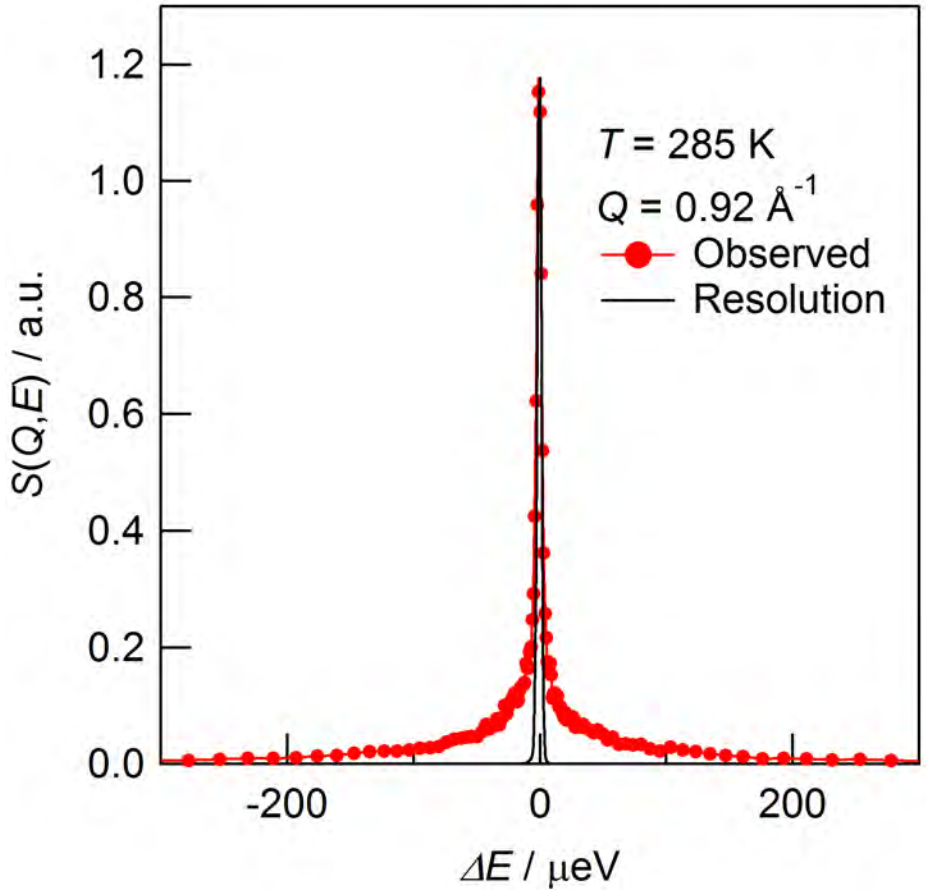
	Coherent scatt.	Incoherent scatt.
DMPC	374.5 barn (5.5%)	5779.3 barn (84.5%)
35D_2O	535.6 barn (7.9%)	143.5 barn (2.1%)

Sample can：14mm-φ / 40mm-h / 0.5mm-t (double cylinder)

QENS data of $d_{67}DMPC\text{-}37H_2O$

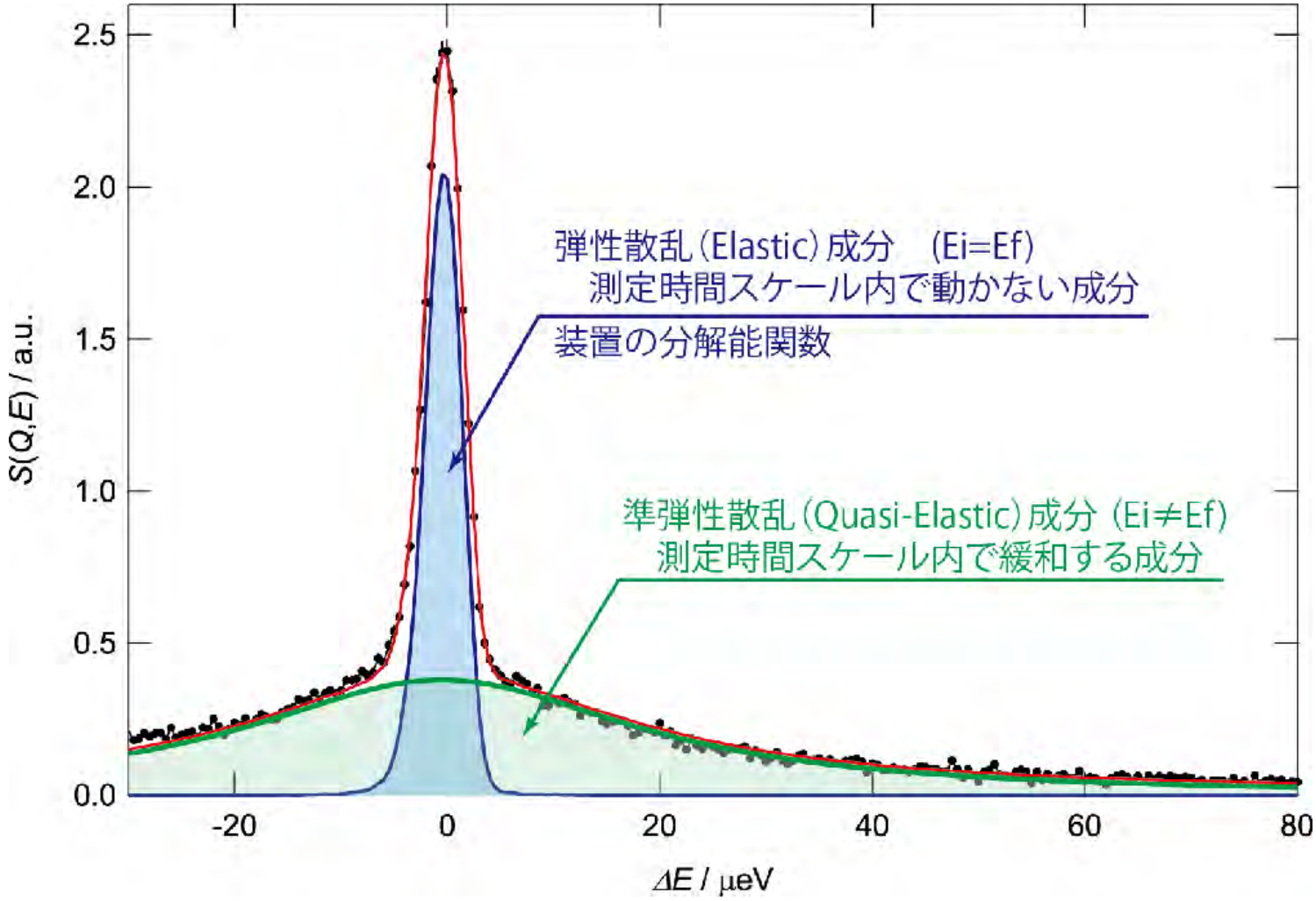
dynamics of water molecules





Quasi-Elastic Neutron Scattering was observed and its width increased with increasing temperature.

QENS profiles



Horizontal axis: energy transfer ($\Delta E = E_i - E_f$)

large ΔE (wide Half Width at Half Maximum: fast motion
small ΔE (narrow Half Width at Half Maximum: slow motion

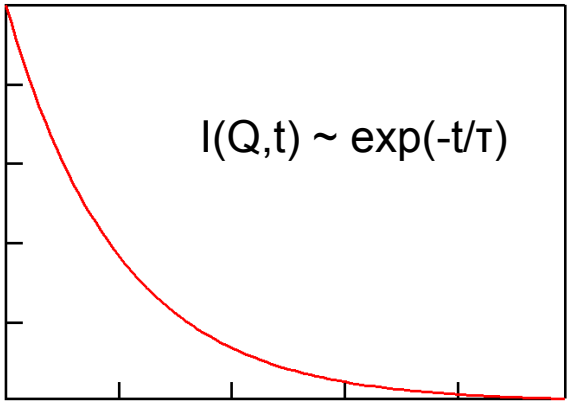
散乱プロファイルの解析

ローレンツ関数

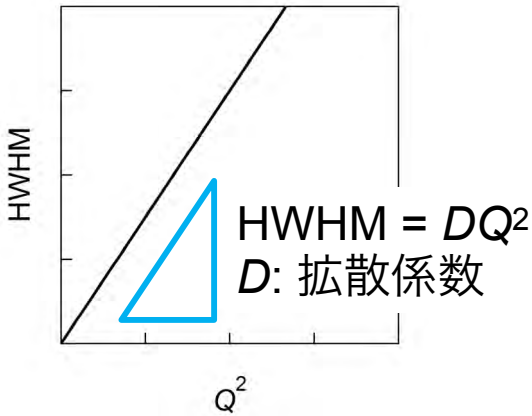
半値半幅（HWHM）

$$f(\Delta E,\tau) = \frac{\left(\frac{1}{\tau}\right)}{\Delta E^2 + \left(\frac{1}{\tau}\right)^2}$$

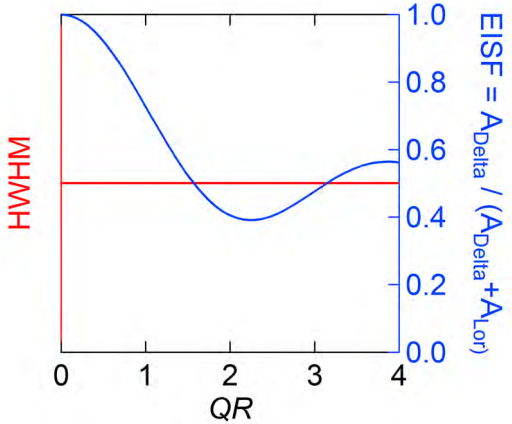
フーリエ変換



半値半幅のQ依存性

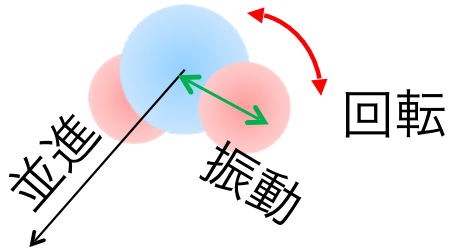


拡散運動



局所運動

分子の運動

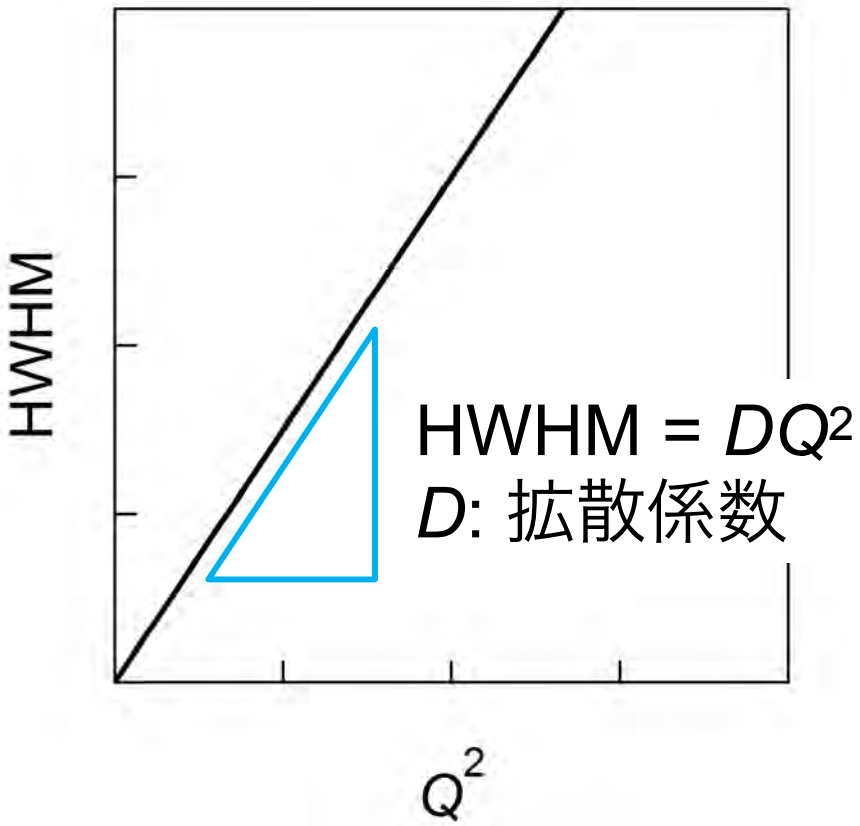


特徴付けるパラメーター

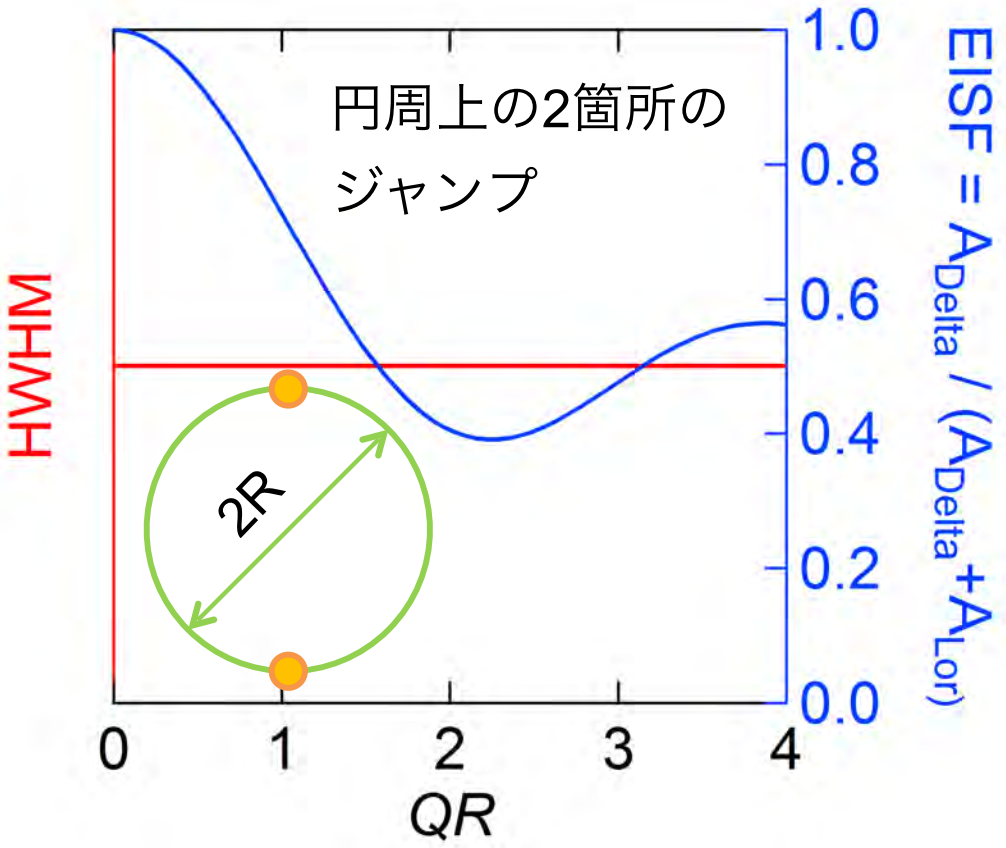
緩和時間、拡散距離、回転半径

分子運動と半値半幅の関係

拡散運動

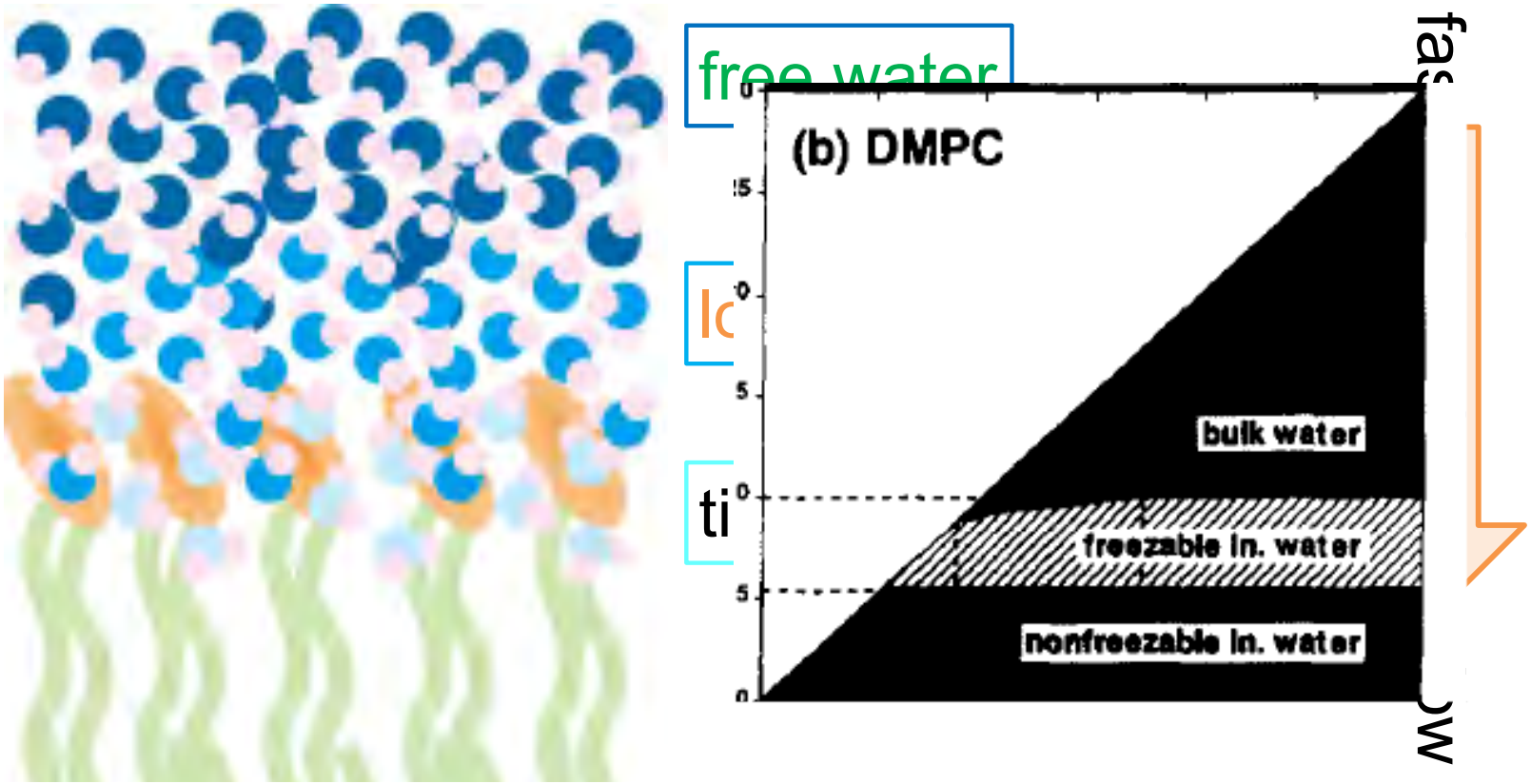


局所運動



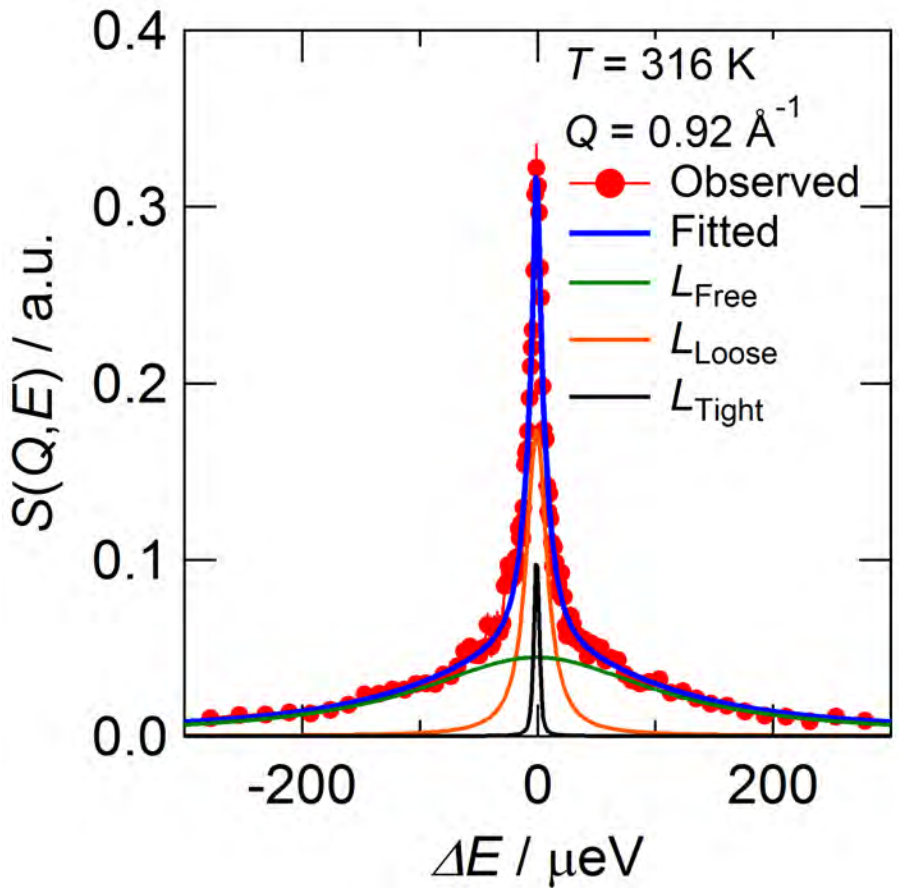
中性子準弾性散乱プロファイルを解析すると分子のダイナミクスが分かる

Model Analysis



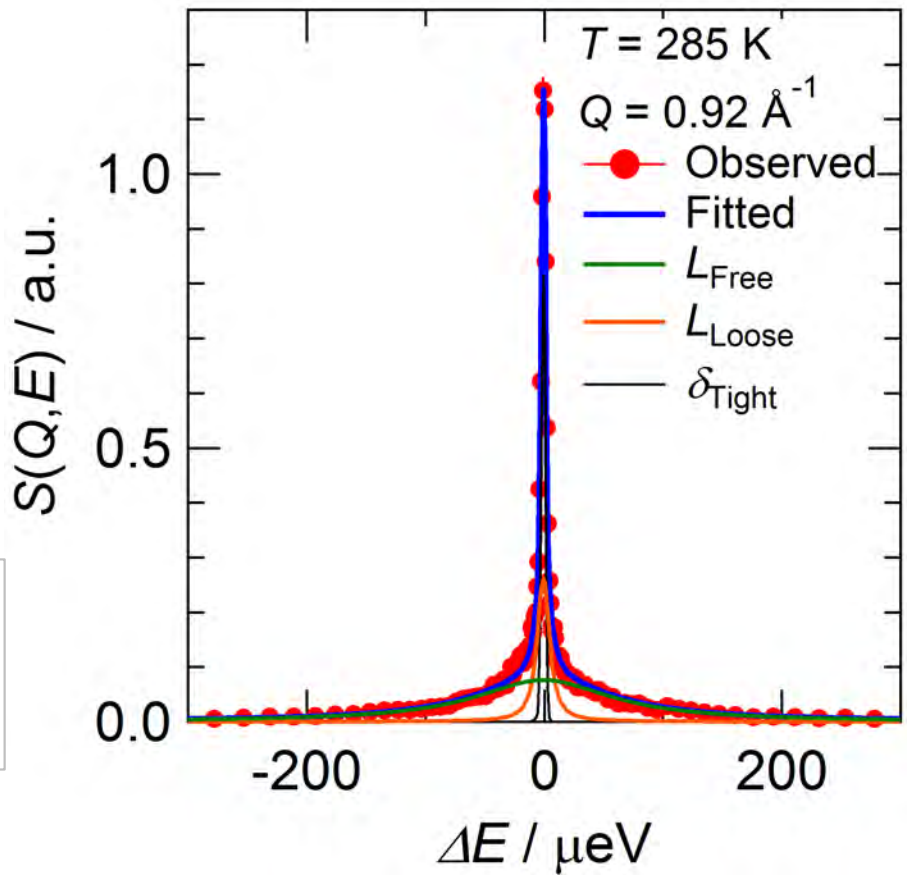
3 modes are assumed to analyze the observed QENS data

Liquid Crystalline Phase
(*T* = 316, 305, 295)



$$S(Q,E) = [A_{Tight}L_{Tight}(E) + A_{Loose}L_{Loose}(\Gamma_{Loose},E) + A_{Free}L_{Free}(\Gamma_{Free},E)] \otimes R(Q,E) + BG$$

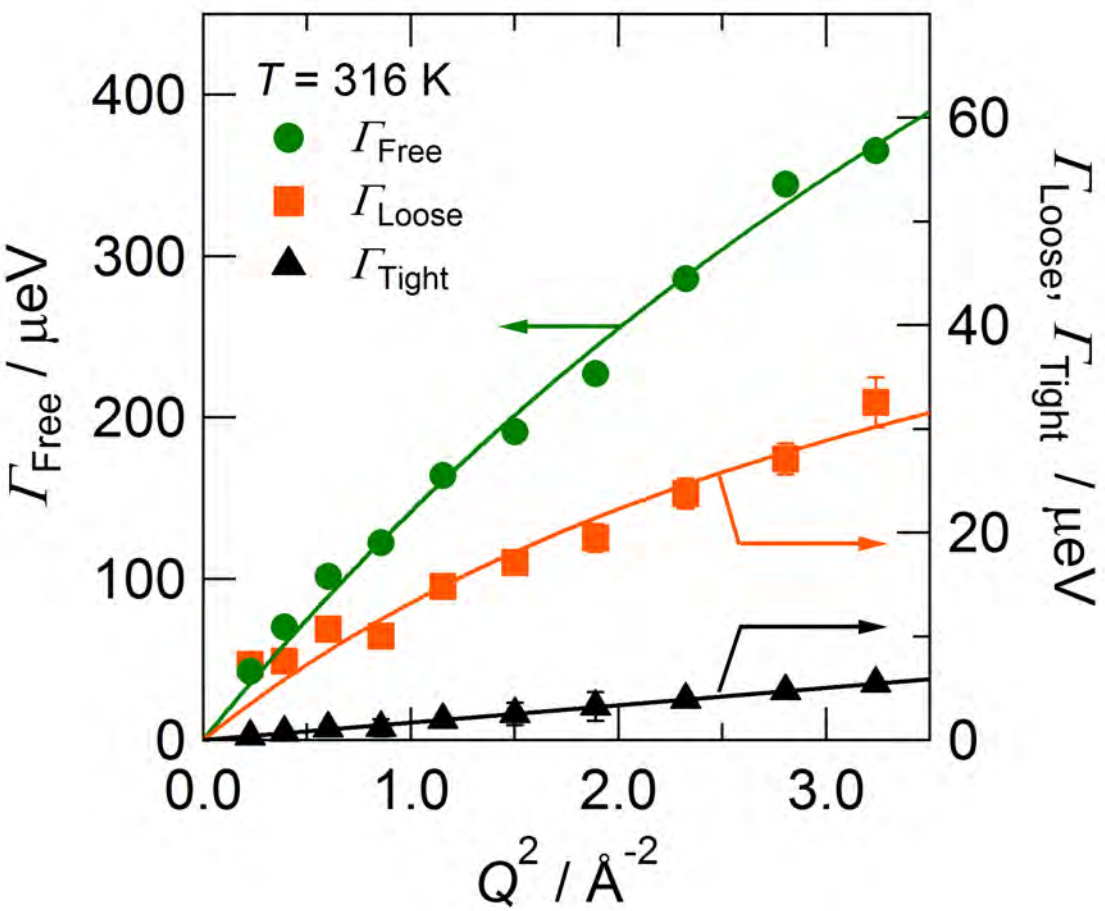
Ripple Gel Phase & Gel Phase
(T = 285, 275 K)



Tightly bound water is too fast to observe (the width is less than the resolution function).

$$S(Q,E) = [A_{Tight}\delta_{Tight}(E) + A_{Loose}L_{Loose}(\Gamma_{Loose},E) + A_{Free}L_{Free}(\Gamma_{Free},E)] \otimes R(Q,E) + BG$$

Q^2 dependence of HWHM



Tightly bound water

Simple diffusion model (Fick's law)

$$\Gamma_{\mathrm{Tight}} = DQ^2$$

Loosely bound water

Free water

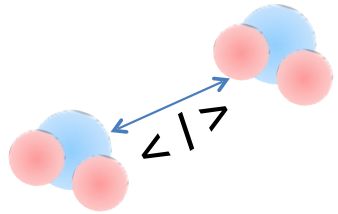
Jump diffusion model

$$\Gamma = \frac{DQ^2}{1+DQ^2\,\tau_0}$$

τ_0 : mean residence time

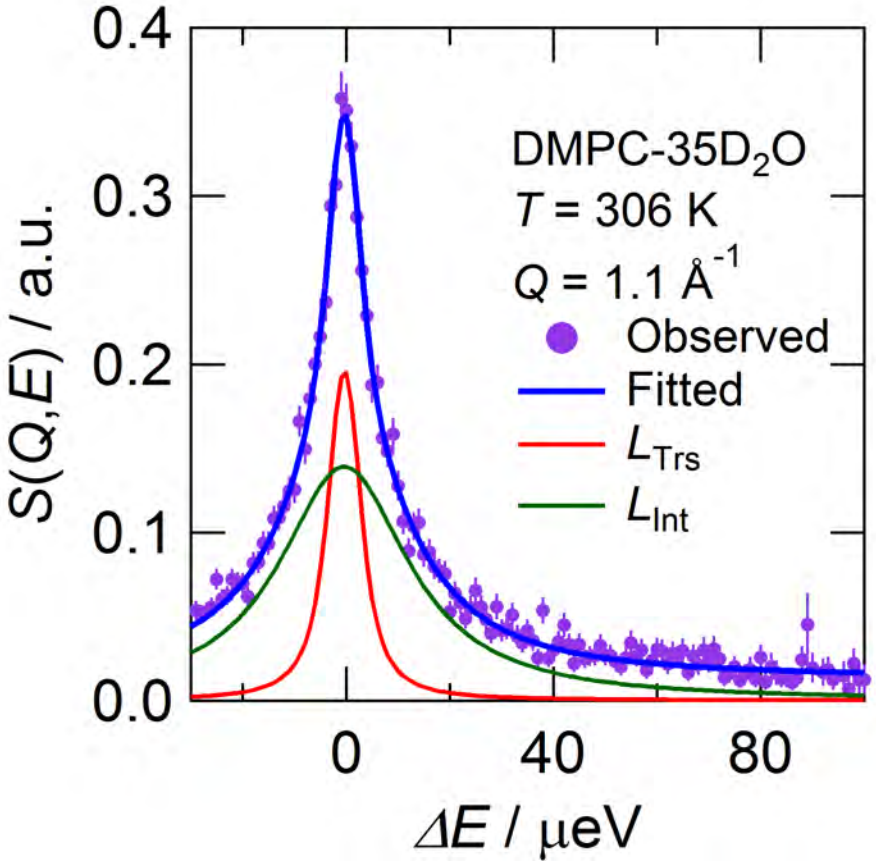
D: diffusion coefficient ($D = \langle l \rangle^2/6\tau_0$)

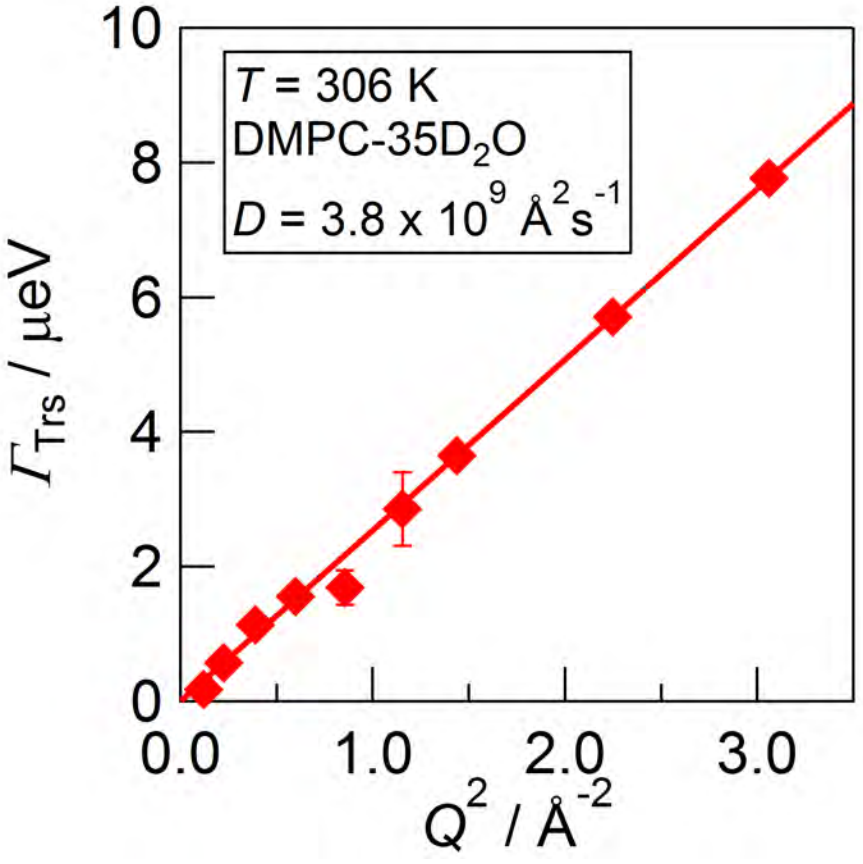
$\langle l \rangle$: jump distance



QENS data of DMPC-35D_2O

Dynamics of lipid molecules



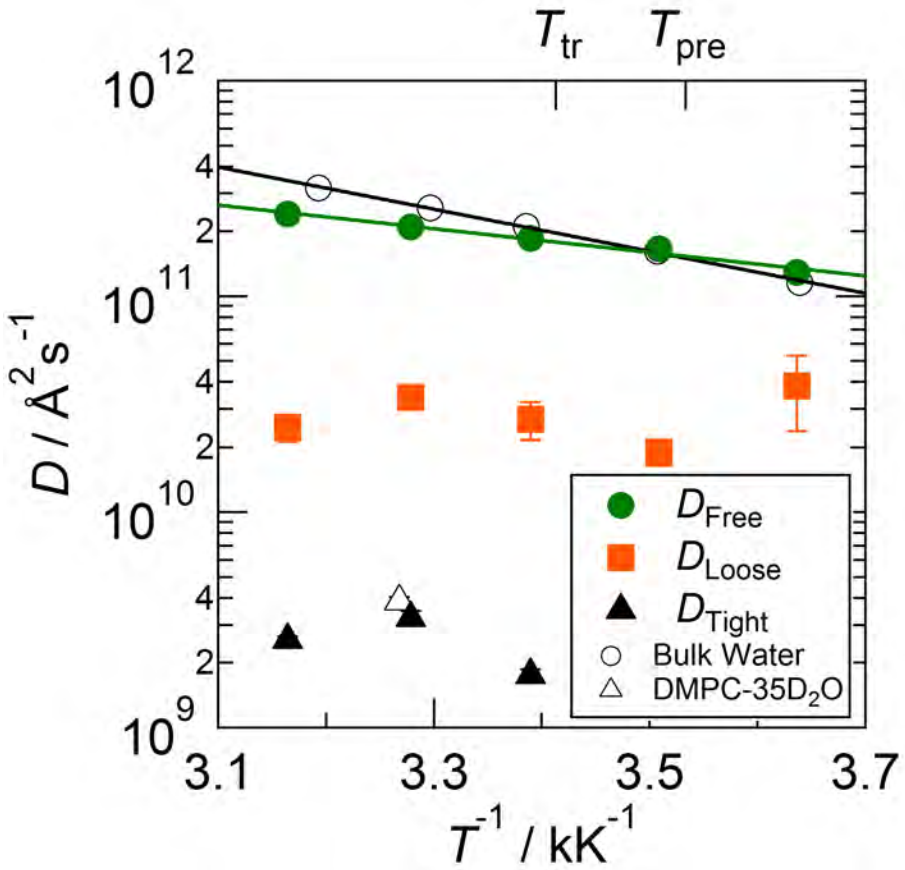


$$S(Q,E) = [A_{Trs}L_{Trs}(\Gamma_{Trs},E) + A_{Int}L_{Int}(\Gamma_{Lat}+\Gamma_{Int},E)] \otimes R(Q,E) + BG$$

A model assuming lateral diffusion of lipid molecules within bilayer and internal mode of a lipid※

※ V. Sharma, et. al, *J. Chem. Phys. B*, **119** (2015), 4460.

Diffusion Coefficient

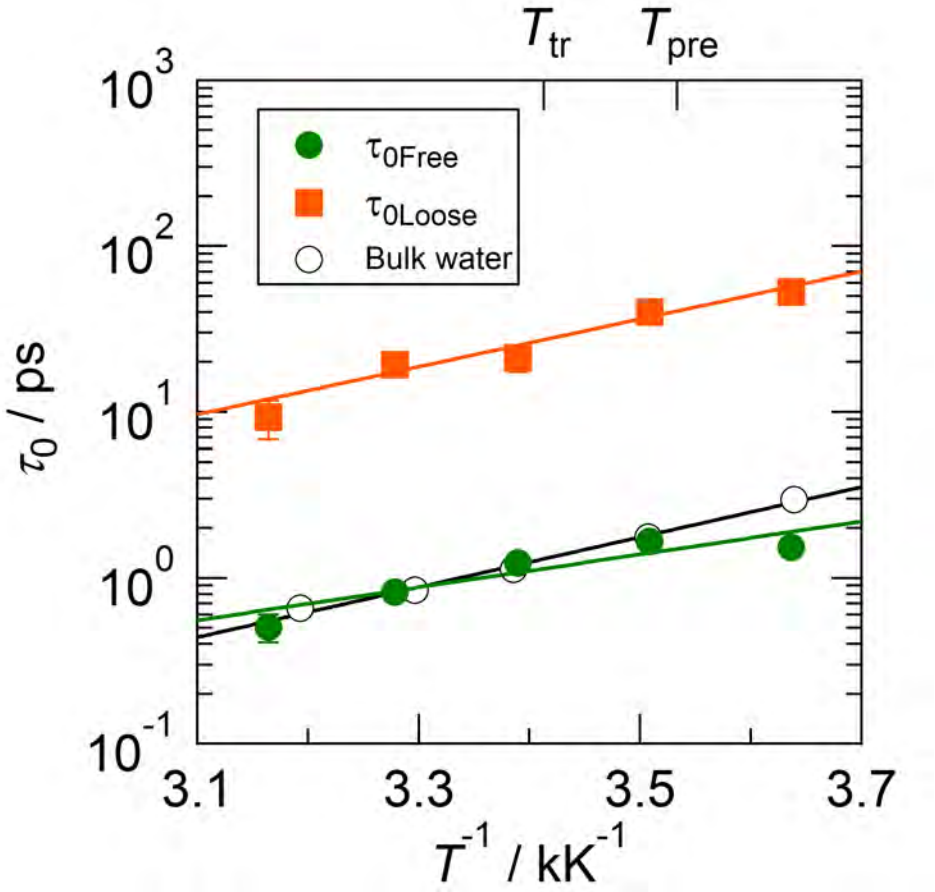


	Activation energy [kJmol^{-1}]
Free water	10.5 ± 1.2
Bulk water	18.6 ± 0.3

Activation energy of “Free water” is less than that of bulk water

Free water: diffusion constant is the same order as that of bulk water
Loosely bound water: 1 order less diffusion constant than that of free water
Tightly bound water: the same diffusion constant as that of DMPC

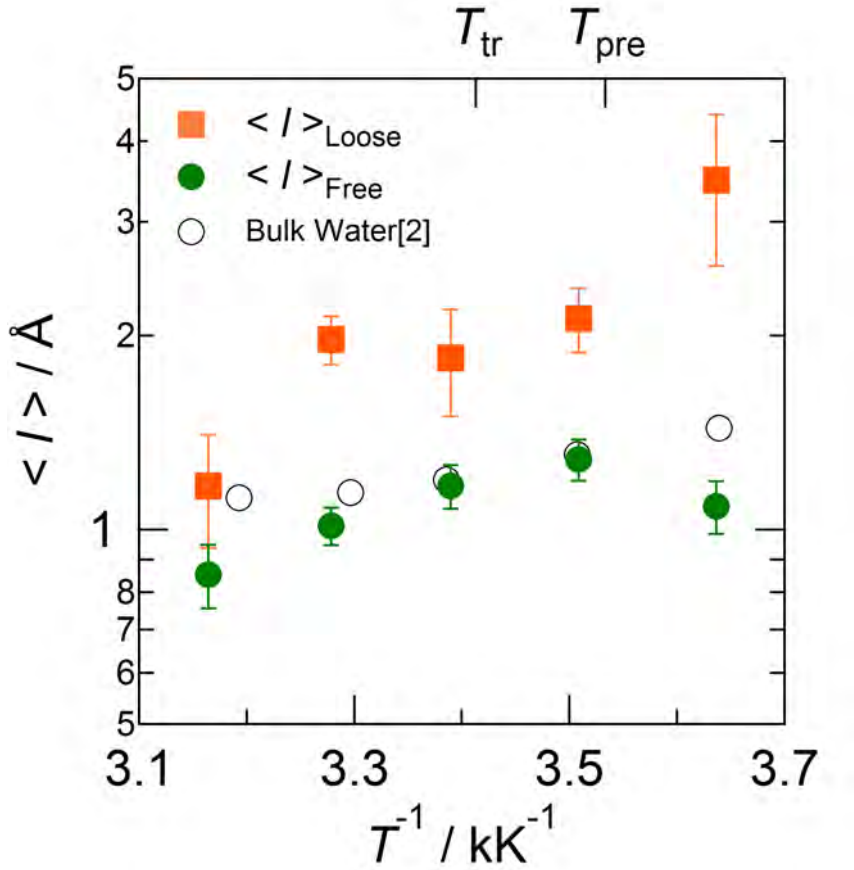
Mean Residence Time



	Activation Energy [kJmol^{-1}]
Free water	19.0 ± 2.5
Bulk water	28.9 ± 1.0
Loosely bound water	27.5 ± 3.2

Free water: mean residence time is the same as that of bulk water
Loosely bound water: 1 order of magnitude more than that of bulk water

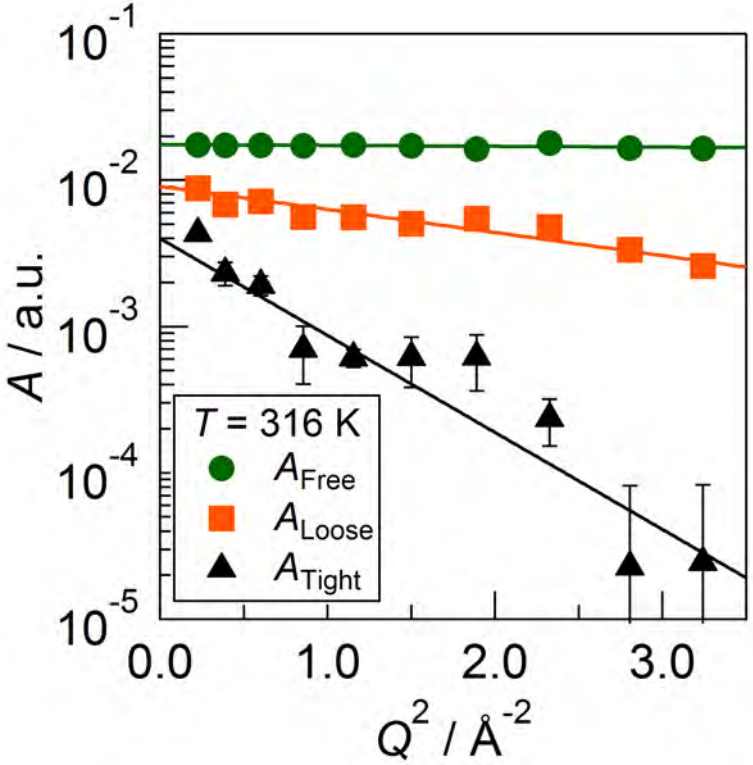
Jump Distance

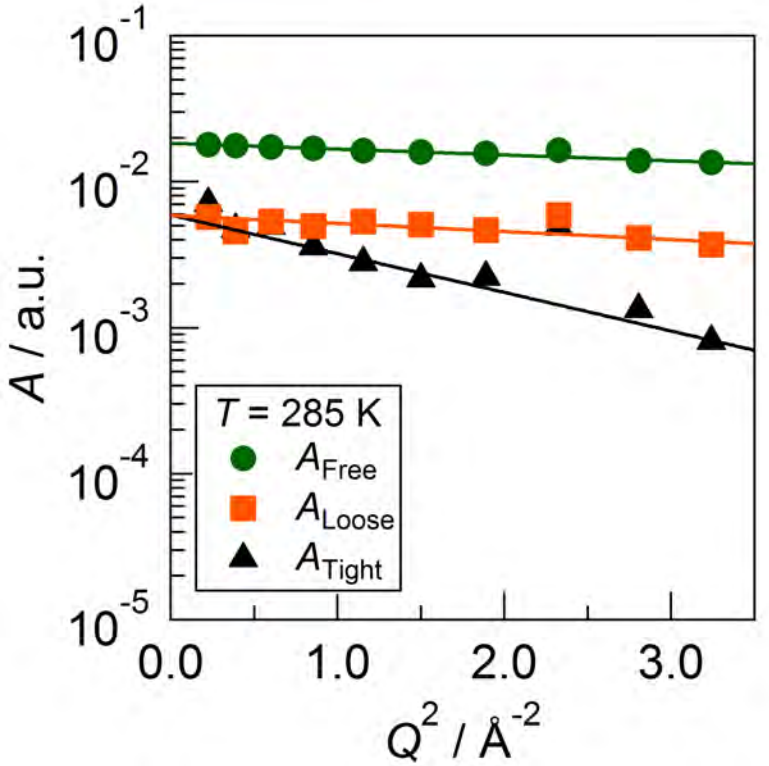


$$D = \frac{\langle l \rangle^2}{6\tau_0}$$

Jump distance of the loosely bound water is longer than that of bulk water
→hydrogen bonding distorts from the normal water structure

Coefficients of 3 components





$$A = A_0 \exp\left(-\frac{\langle u \rangle^2 Q^2}{3}\right)$$

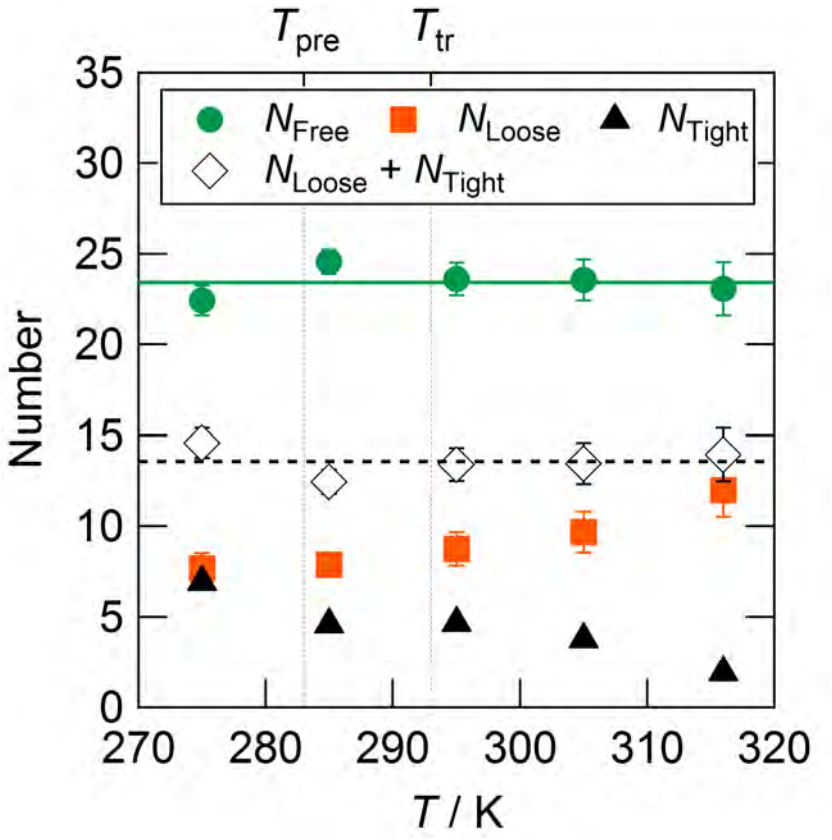
A_0's are proportional to the number of atoms.

Number of water molecules

$$N_{\mathrm{Tight}} = \left(\frac{A_{0\mathrm{Tight}}}{A_{0\mathrm{Tight}} + A_{0\mathrm{Loose}} + A_{0\mathrm{Free}}} - f_{\mathrm{DMPC}} \right) \times \frac{R}{1 - f_{\mathrm{DMPC}}}$$

$$N_{\mathrm{Loose}} = \left(\frac{A_{0\mathrm{Loose}}}{A_{0\mathrm{Tight}} + A_{0\mathrm{Loose}} + A_{0\mathrm{Free}}} \right) \times \frac{R}{1 - f_{\mathrm{DMPC}}}$$

$$N_{\mathrm{Free}} = \left(\frac{A_{0\mathrm{Free}}}{A_{0\mathrm{Tight}} + A_{0\mathrm{Loose}} + A_{0\mathrm{Free}}} \right) \times \frac{R}{1 - f_{\mathrm{DMPC}}}$$



R = 37 (water molecules/lipid molecule)

f_{DMPC} = 0.083

（Incoherent scatt. fraction of DMPC)

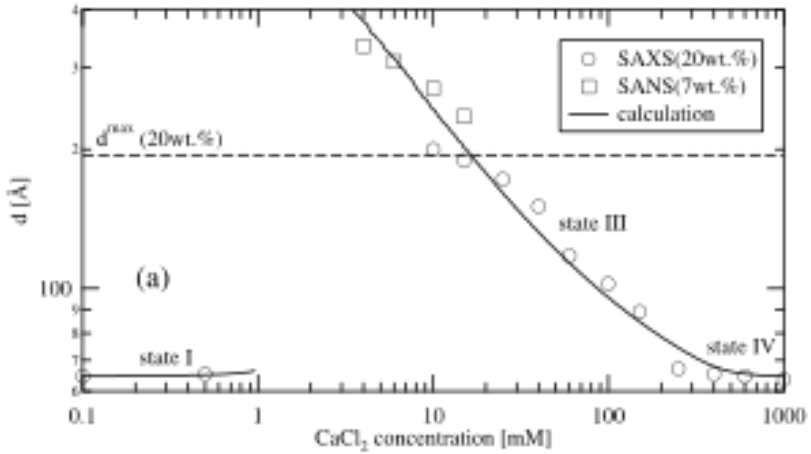
Free water: almost constant

Loosely bound water: increase with increasing temperature

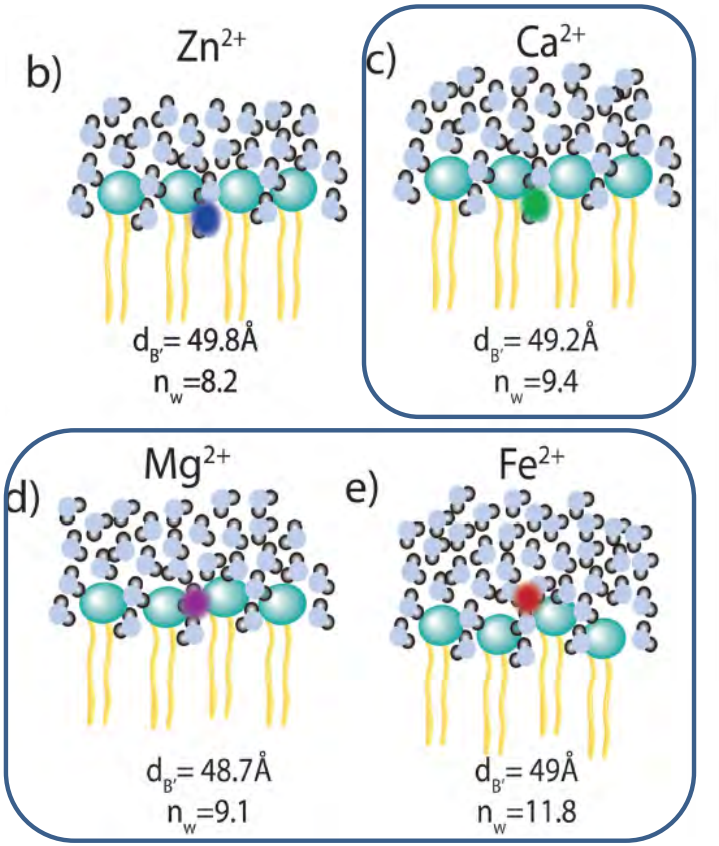
Tightly bound water: decrease with increasing temperature

Effect of Salt on hydration water?

The swelling of phospholipid membranes by adding divalent metal ions have been known.



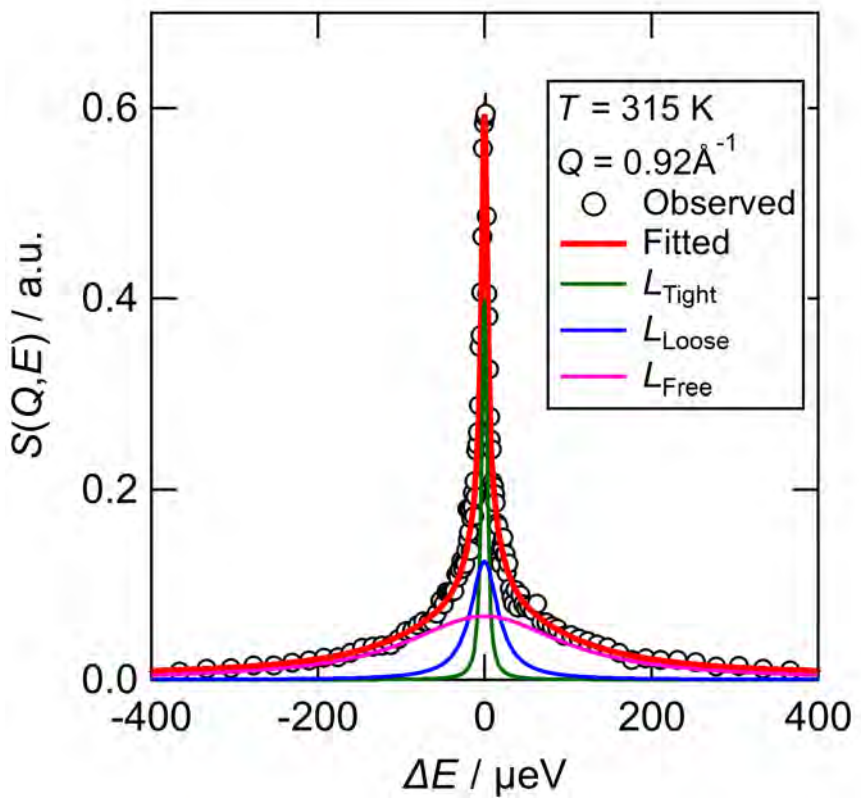
N. L .Yamada, et al. *J. Phys. Soc. Jpn.,* 2005



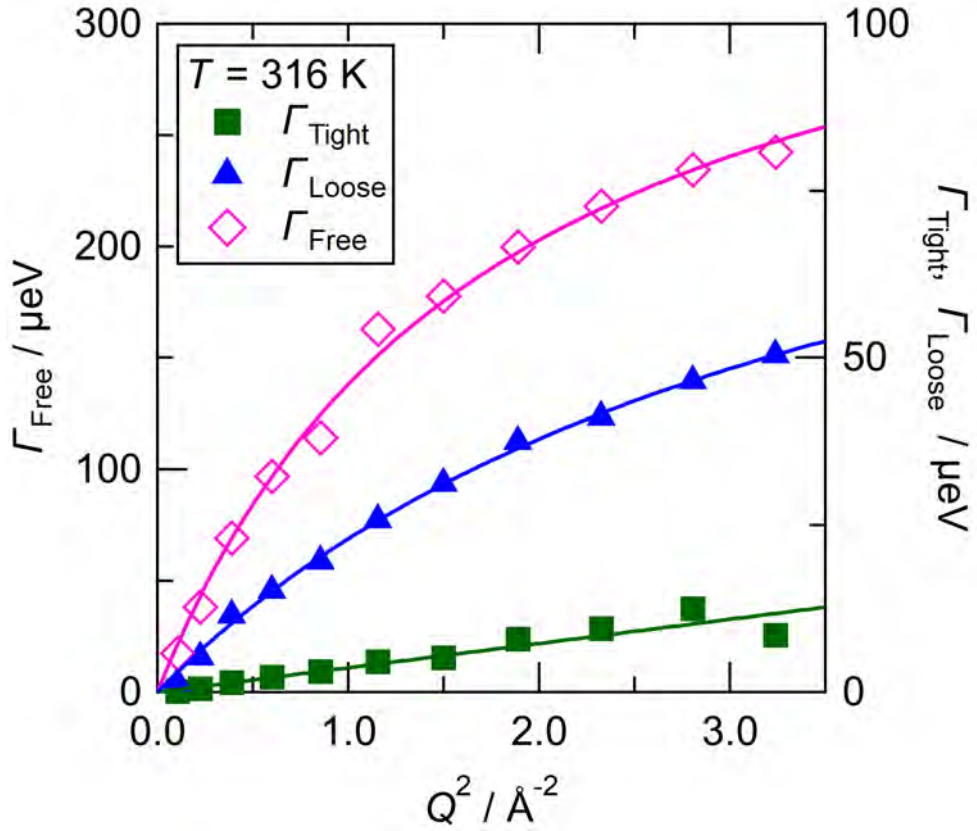
R. J. Alsop, et al. *Soft Matter,* 2016

QENS spectra and analysis

QENS profile of
d_{67}DMPC-37H_2O-0.25$CaCl_2$



Q^2 dependence of Γ



QENS profiles were well analyzed as d_{67}DMPC-37H_2O.

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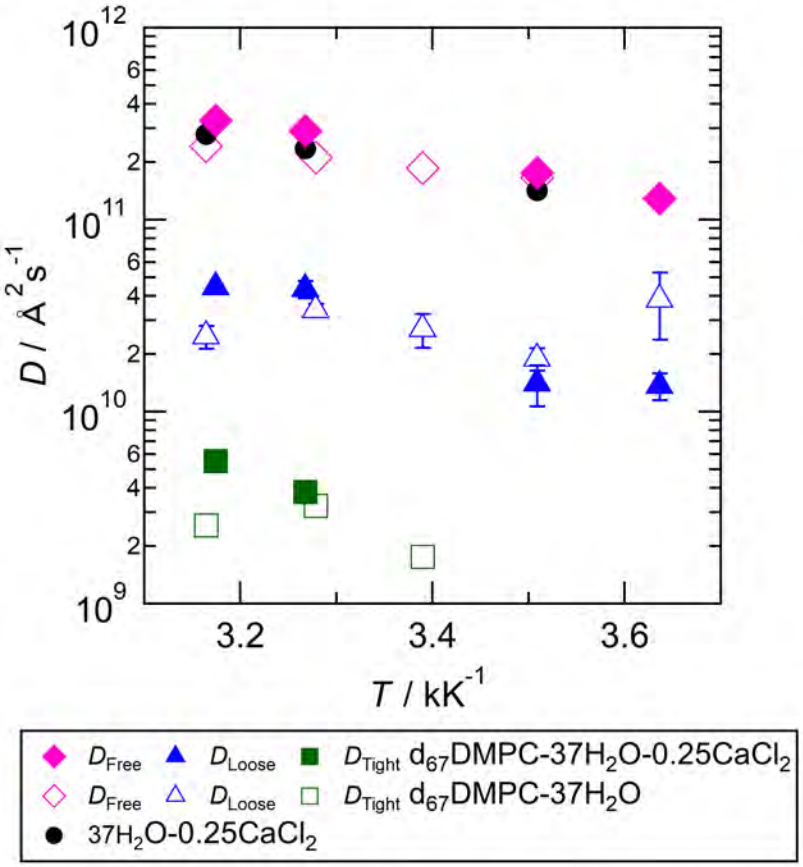
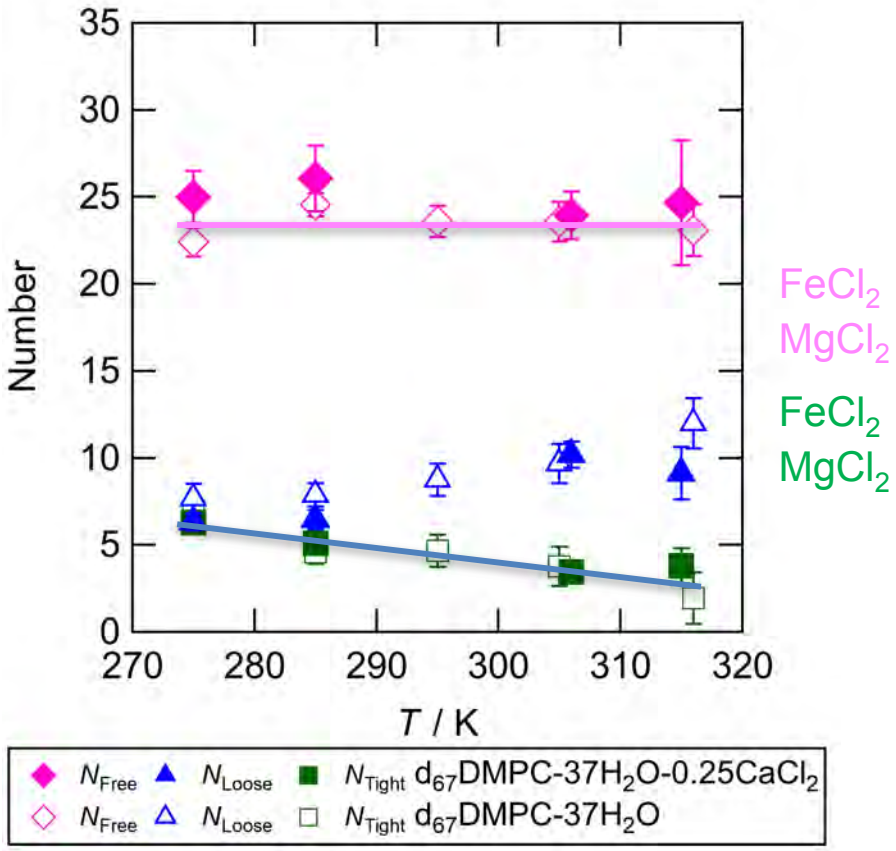
Results

Diffusion coefficients



Number of hydration water



Effect of Ca^{2+} on dynamics of hydration water is small.

Number of tightly bound water increases in the Fe^{2+} and Mg^{2+} cases?

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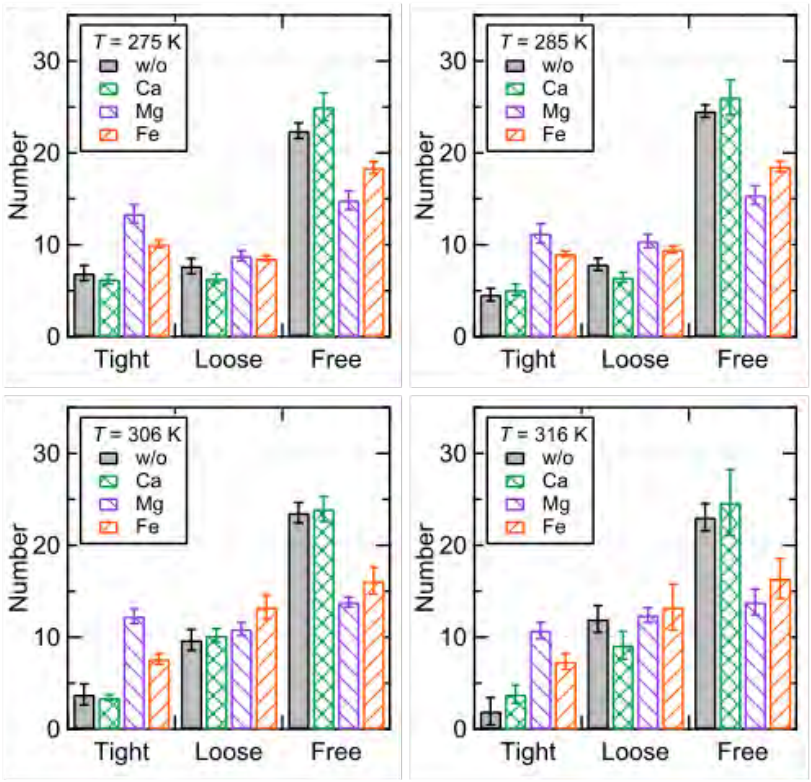
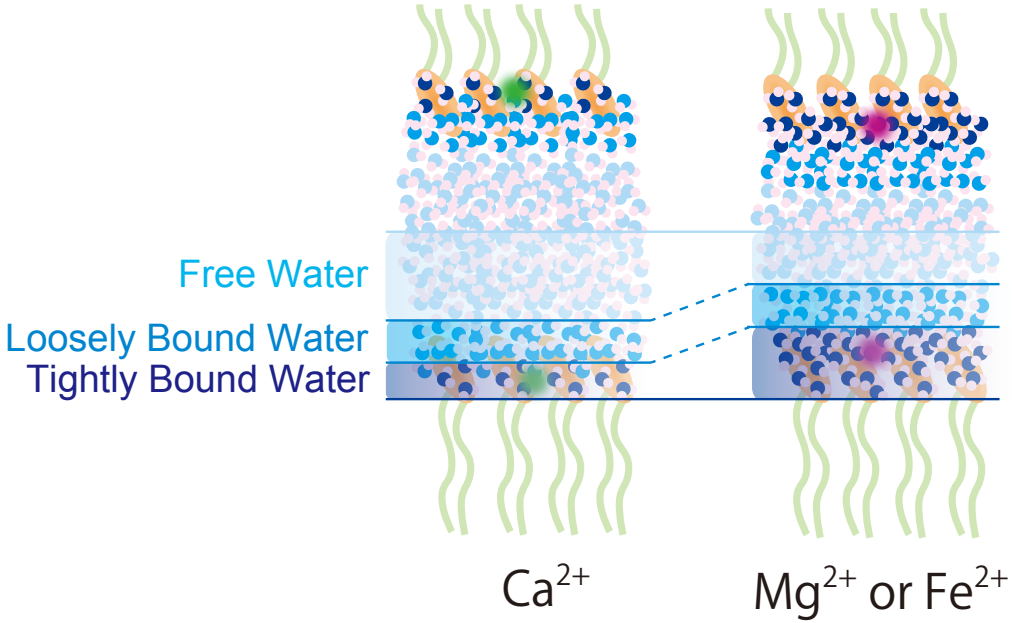
Effect of adding salts: $CaCl_2$, $MgCl_2$ and $FeCl_2$





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H. Seto and T. Yamada, *Appl. Phys. Lett.*, 2020

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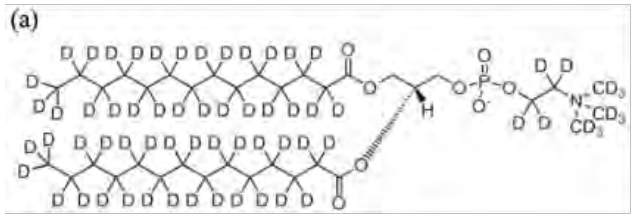
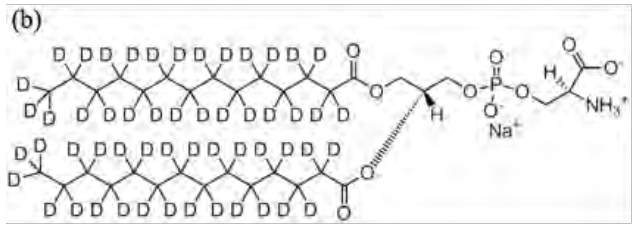
Effect of charged lipids





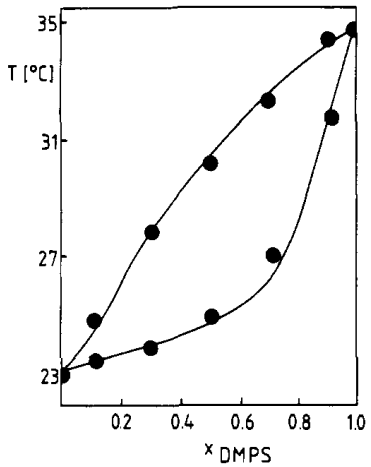


FIGURE 1: Phase diagram of a mixture of DMPC and DMPS. The circles give the positions of the phase boundaries as determined from the molar volume vs. temperature plots following Schmidt and Knoll (1986). The drawn curves were calculated on the basis of the regular solution theory by the computer-fitting procedure described under Discussion. The following values of the transition temperatures and the heats of transition were assumed: DMPC, T_{m_1} = 23 °C; ΔH_1 = 28 kJ M^{-1}. DMPS, T_{m_2} = 35 °C; ΔH_2 = 29.2 kJ M^{-1}.

QENS experiments at T = 323, 316, 309, 305 K

$0.9d_{67}DMPC+0.1d_{54}DMPS+37H_2O$

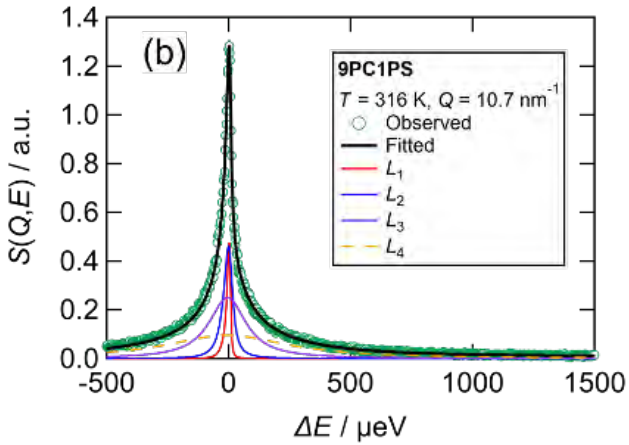
$0.8d_{67}DMPC+0.2d_{54}DMPS+37H_2O$

MD simulation at T = 305 K

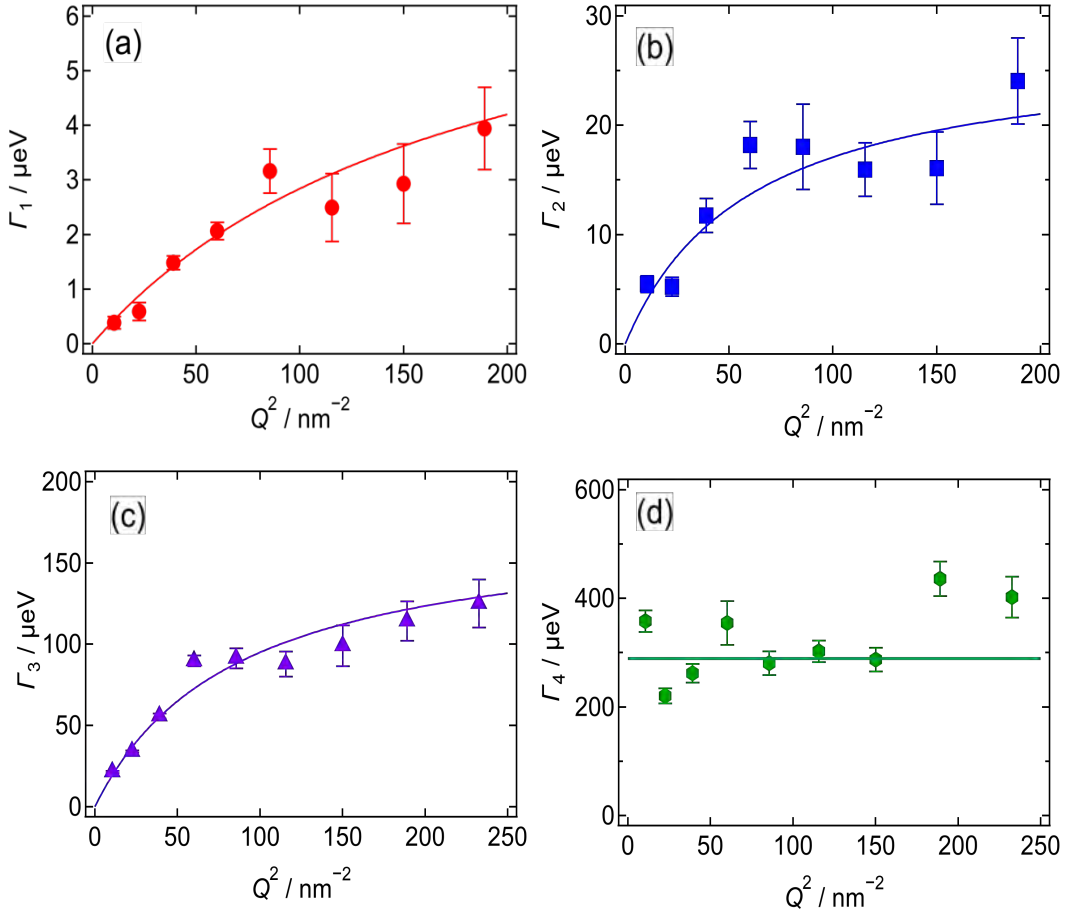
$DMPC+37H_2O$

$0.9DMPC+0.1DMPS+37H_2O$

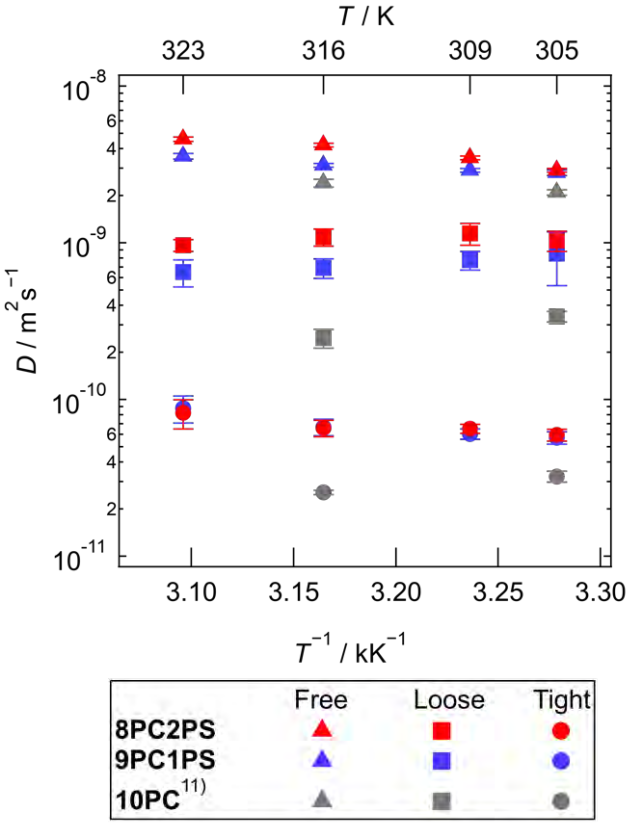
QENS results

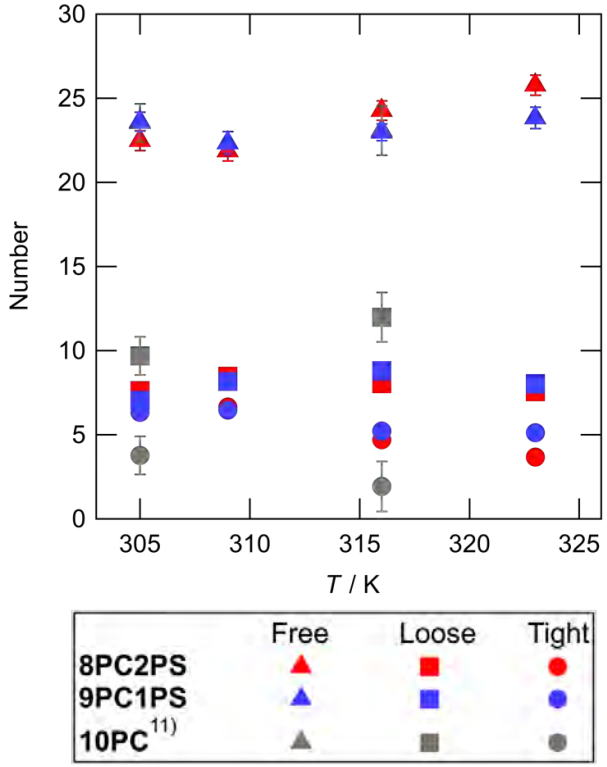


$$S(Q,E) = \{\sum_{i=1}^{n=3 \text{ or } 4} A_i L(\Gamma_i, E)\} \otimes R(Q,E) + BG$$

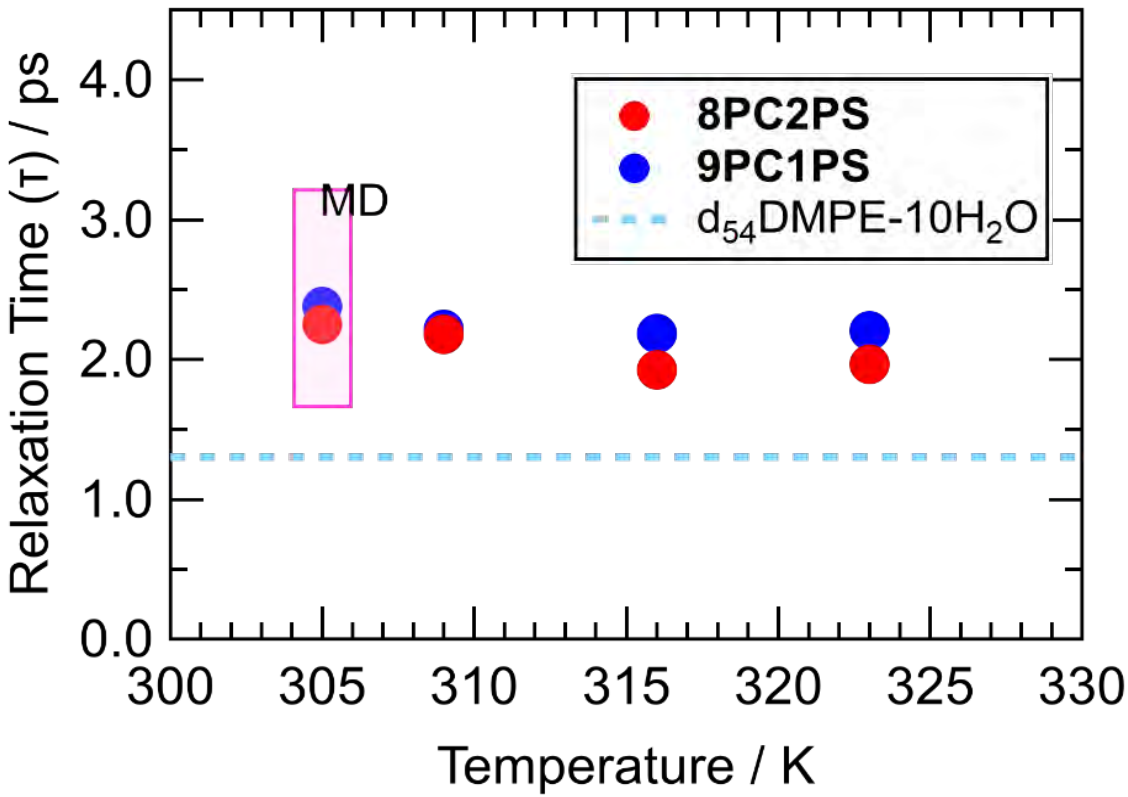


Compared with DMPC results

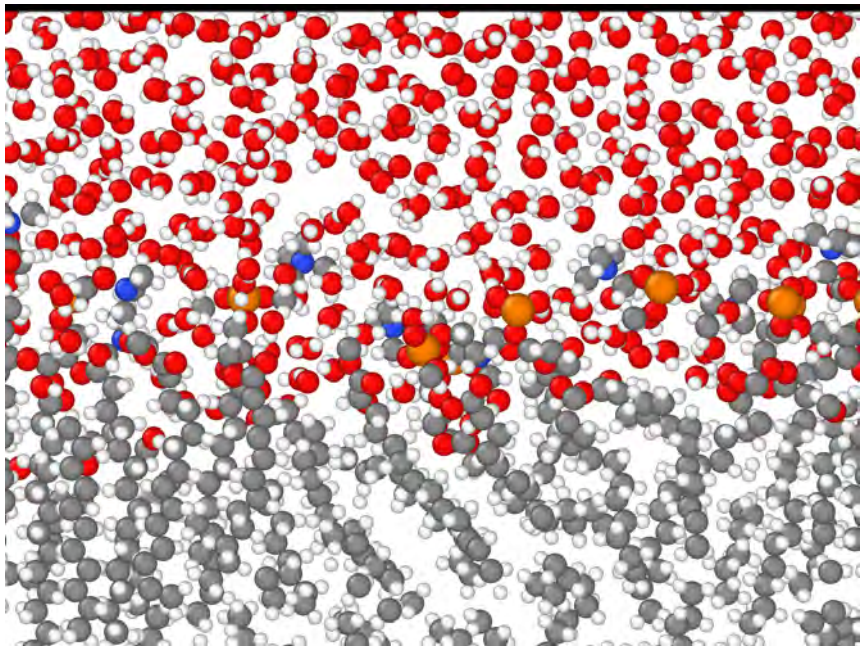


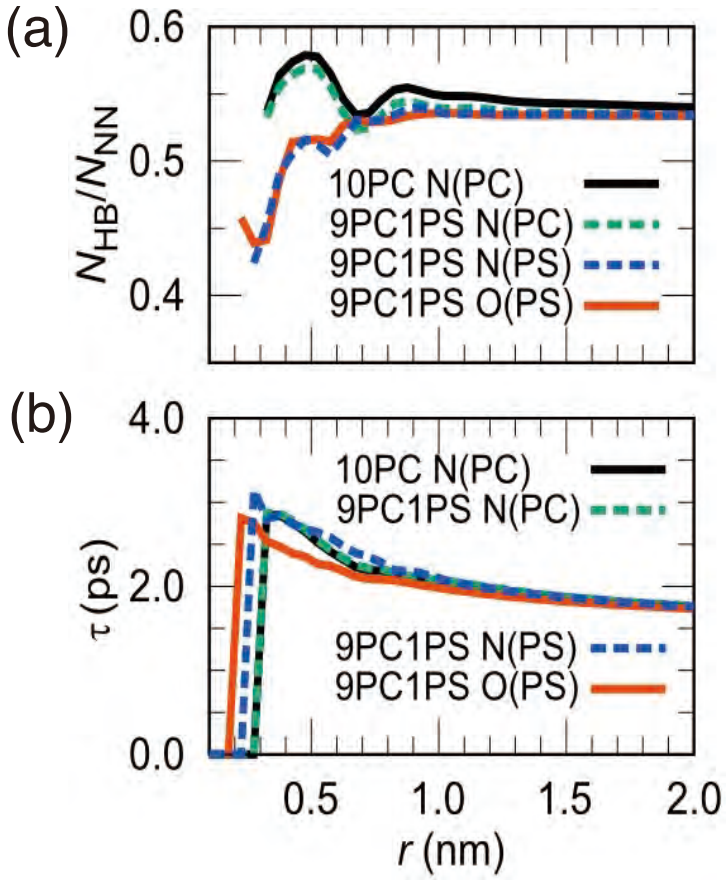


Changes of rotational motions



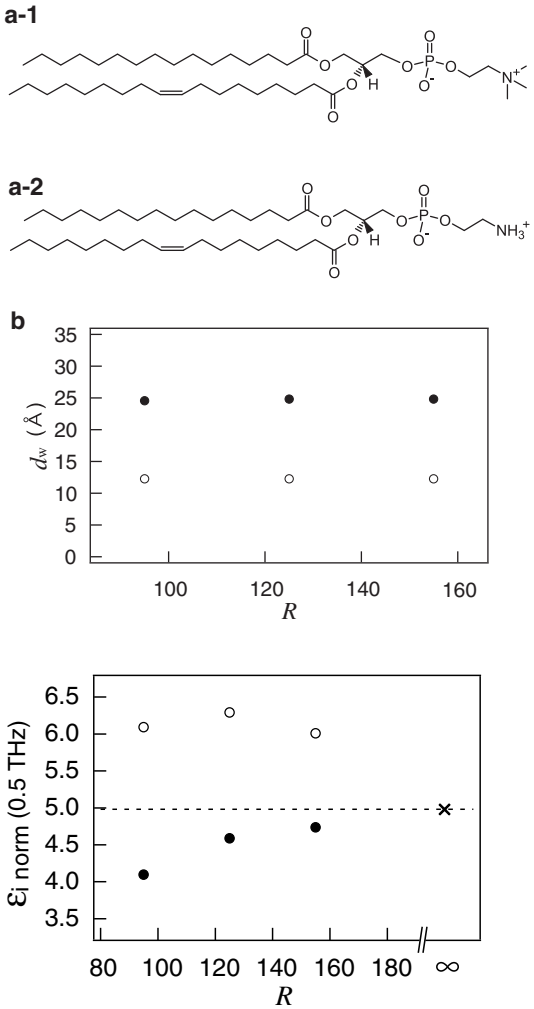
HBs are disrupted around PS



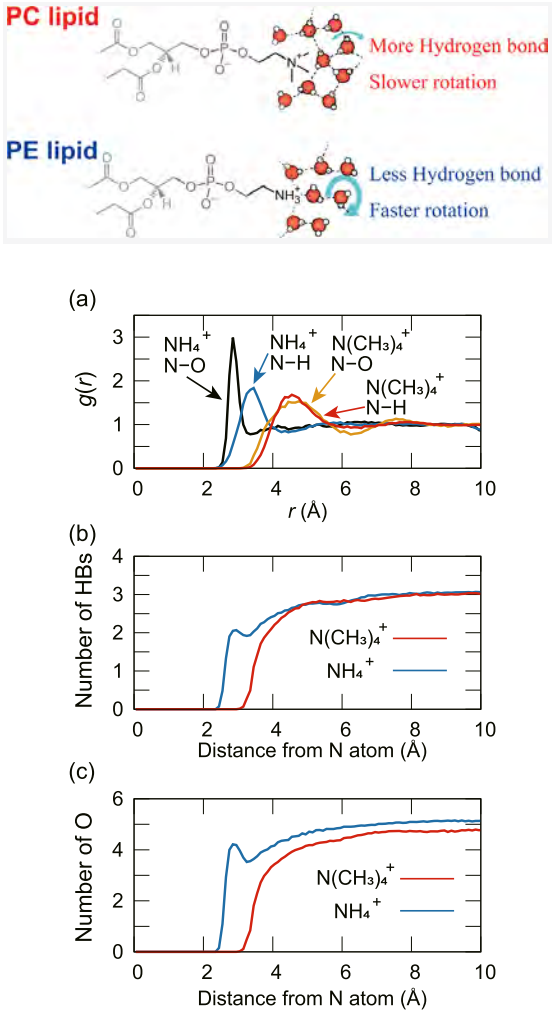


PC lipid and PE lipid

Hishida et al., J. Phys. Soc. Jpn. 2014

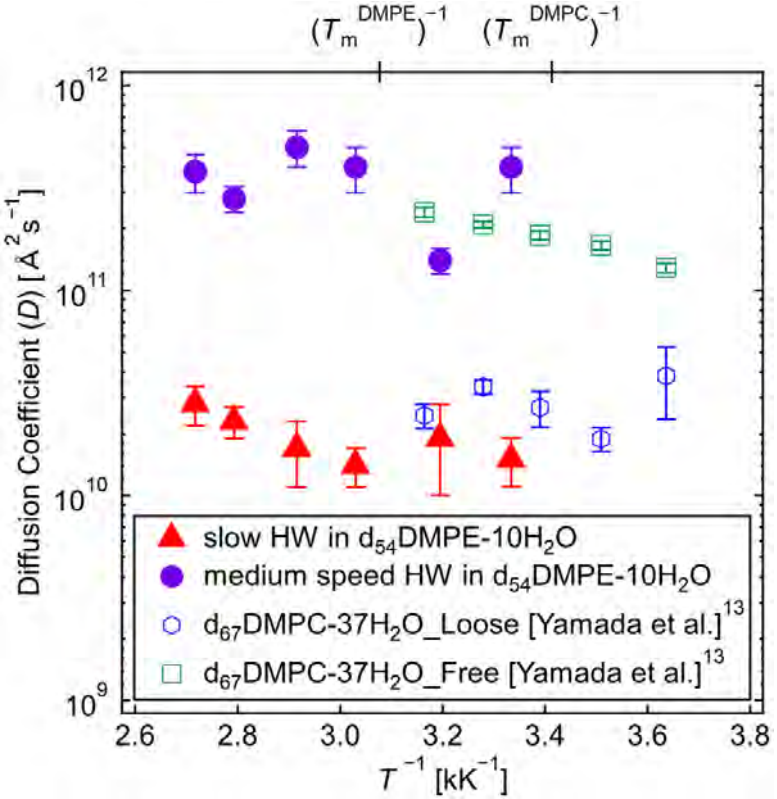


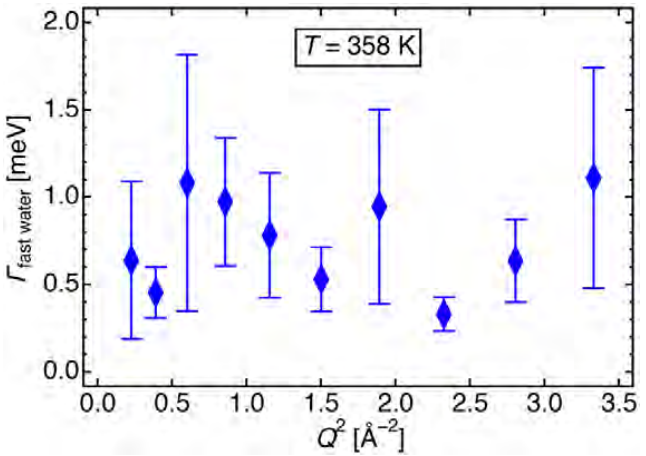
Higuchi et al., Langmuir 2021

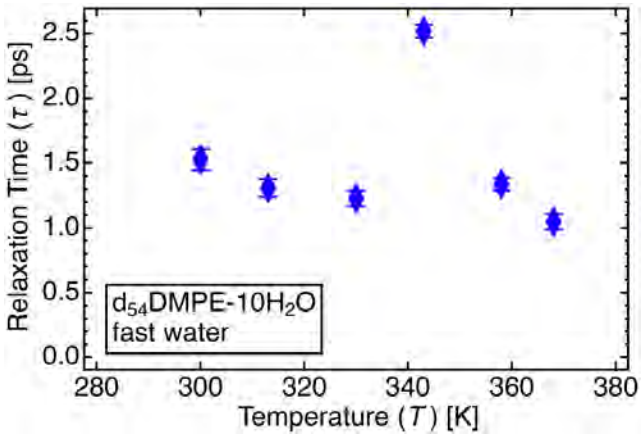


QENS on DMPE+10H_2O

Rahman et al., *Struct. Dyn.* 2023







Summary

free water

24 molecules: no T dependence

nearly bulk water, but confinement effect

loosely bound water

8-12 molecules: increase with T

slow dynamics: 1/10 of free water

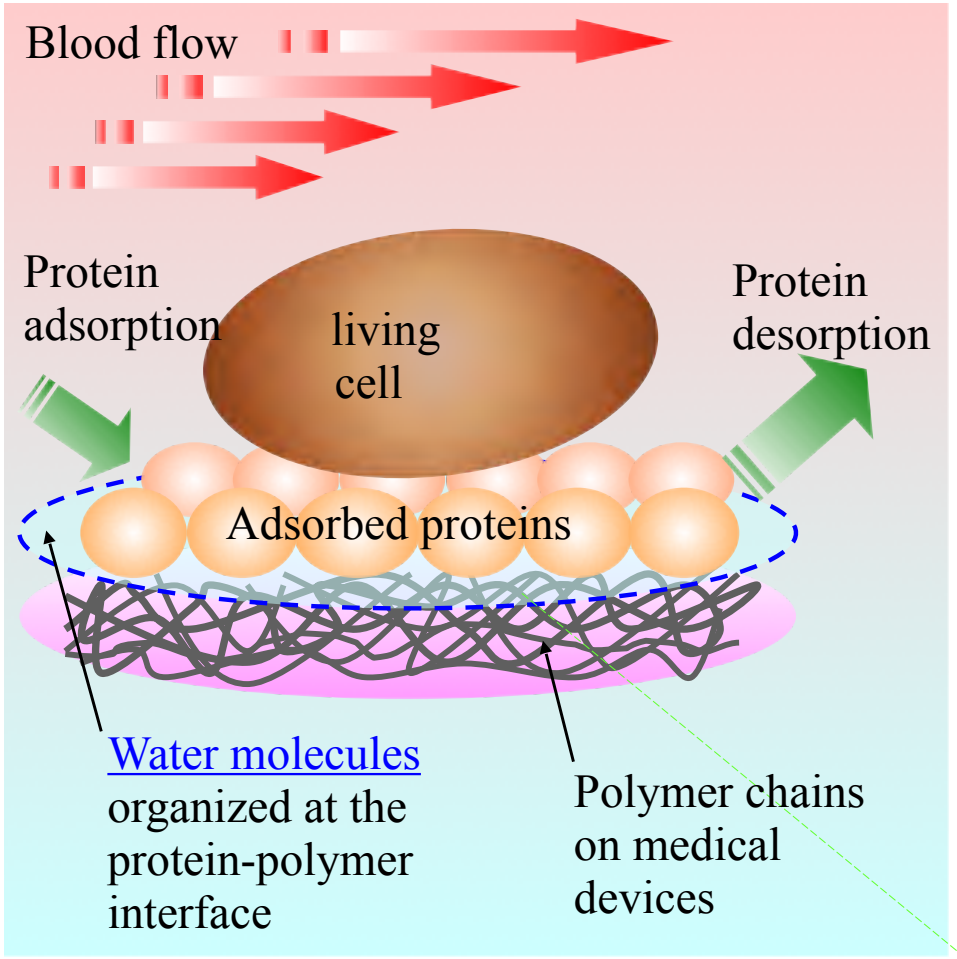
tightly bound water

7-2 molecules: decrease with T, move with lipid molecules, and depends on cation binding

Thick “loosely bound water” layer may relate with biocompatibility and be decided by the nature of lipid headgroups.

Biocompatible polymers

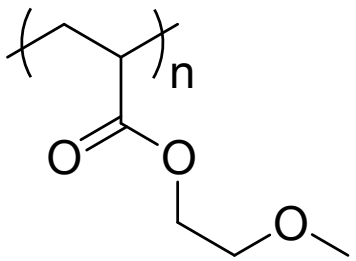
- Biocompatibility
  - properties to prevent blood-clotting / thrombus formation / inhibit the protein adhesion and denaturation
- Utilized as coating materials of biomedical devices
  - blood-contacting medical devices such as artificial organs and blood vessels



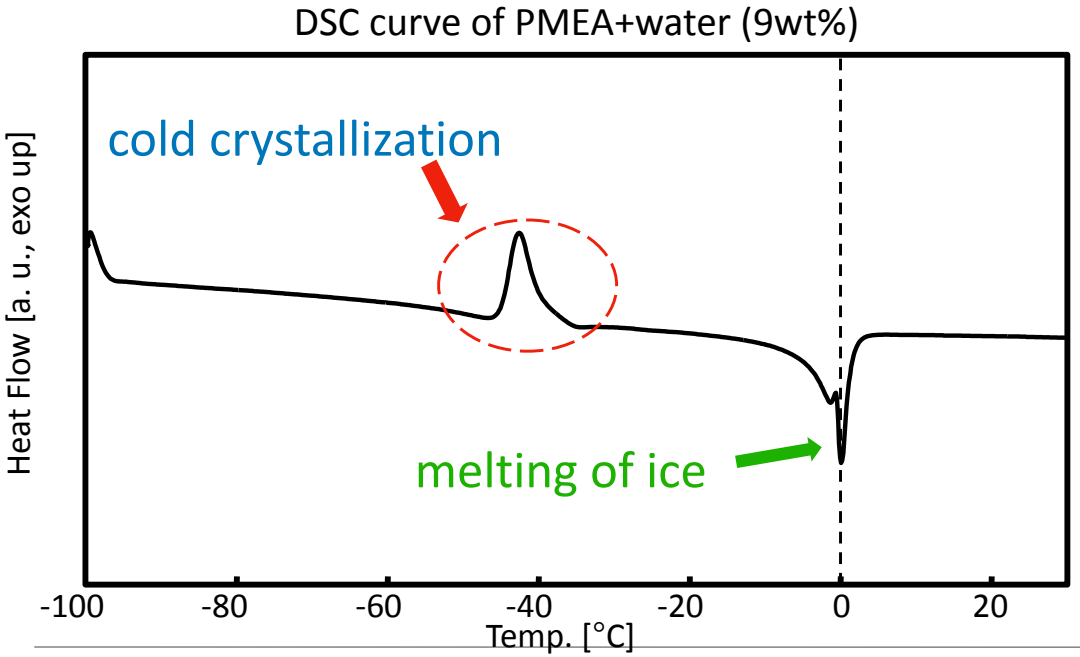
Biocompatibility and cold crystallization

PMEA: poly(2-methoxyethyl acrylate)

- excellent biocompatibility: the largest market share in the world
  - low protein adhesion and denaturation
  - low blood cells adhesion and activation
  - low toxicity
- water insoluble



PMEA



A large cold crystallization peak is considered as a signature of the biocompatibility

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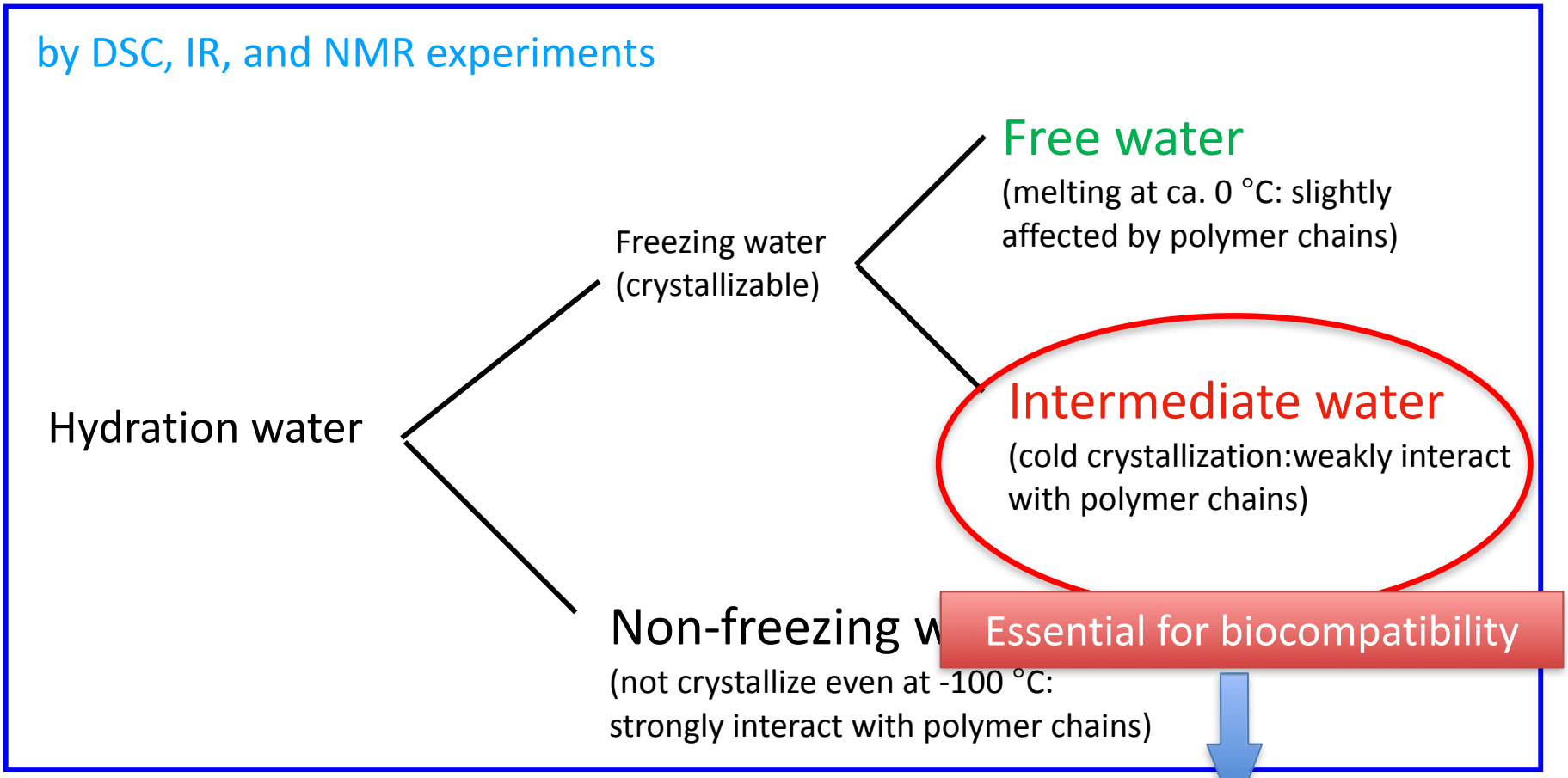
Categorization of hydration water



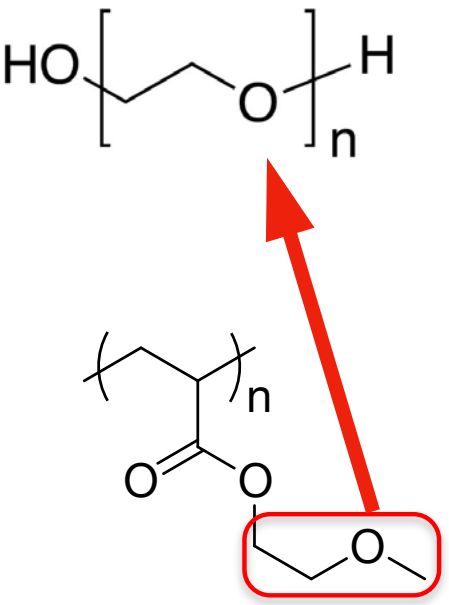
QENS will clarify the relation between polymer chains and water molecules.

What is the origin?
How to control?

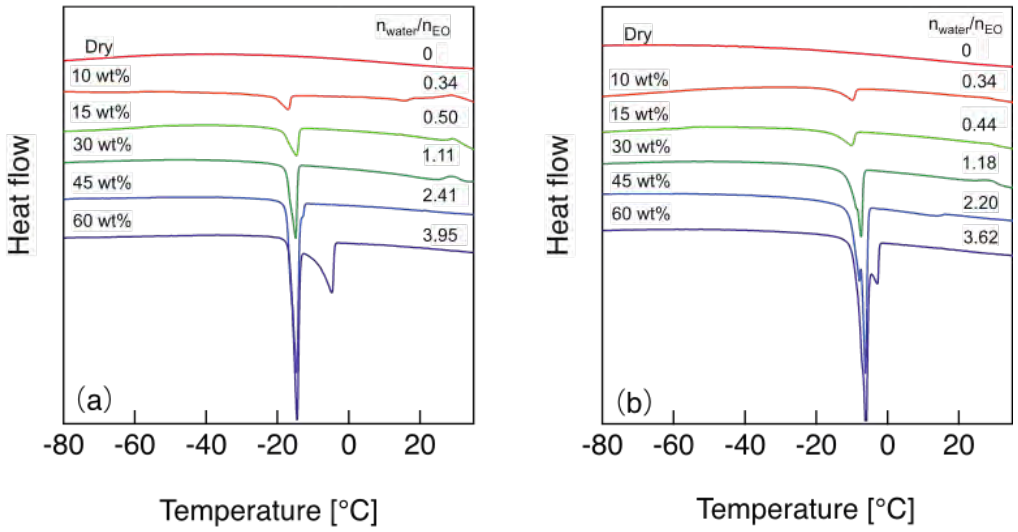
PEO(polyethylene oxide)

T = 37 °C

- typical biocompatible polymer
- “cold crystallization” is already confirmed
- similarity of chemical structure with PMEA
- deuterated PEO is commercially available
- water soluble

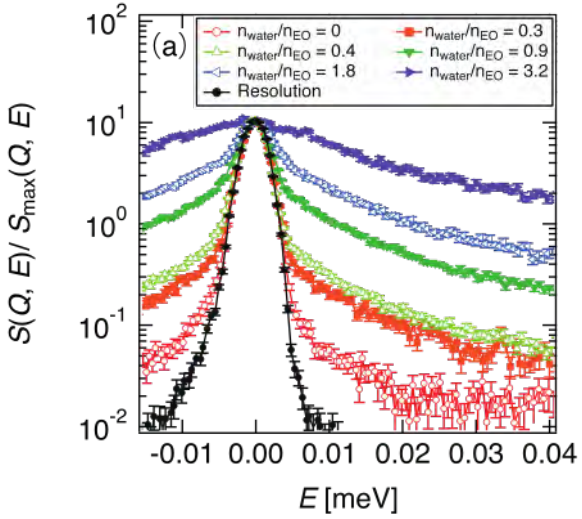


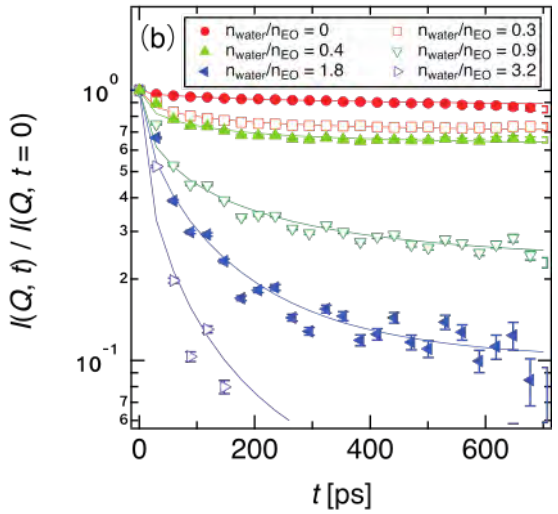
PMEA



DSC curves of (a) *d*PEO/H_2O and (b) *h*PEO/D_2O.

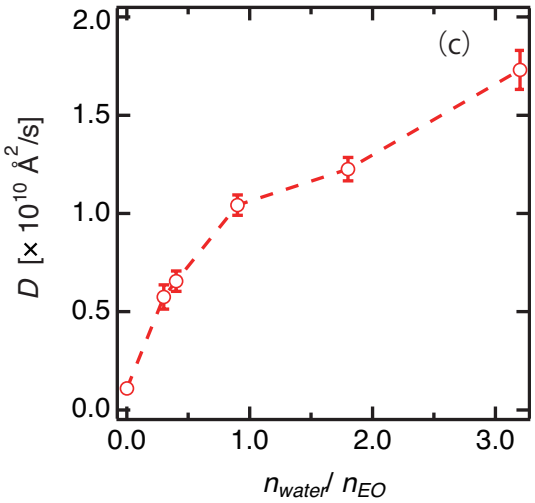
QENS of hPEO/D_2O: polymer motion





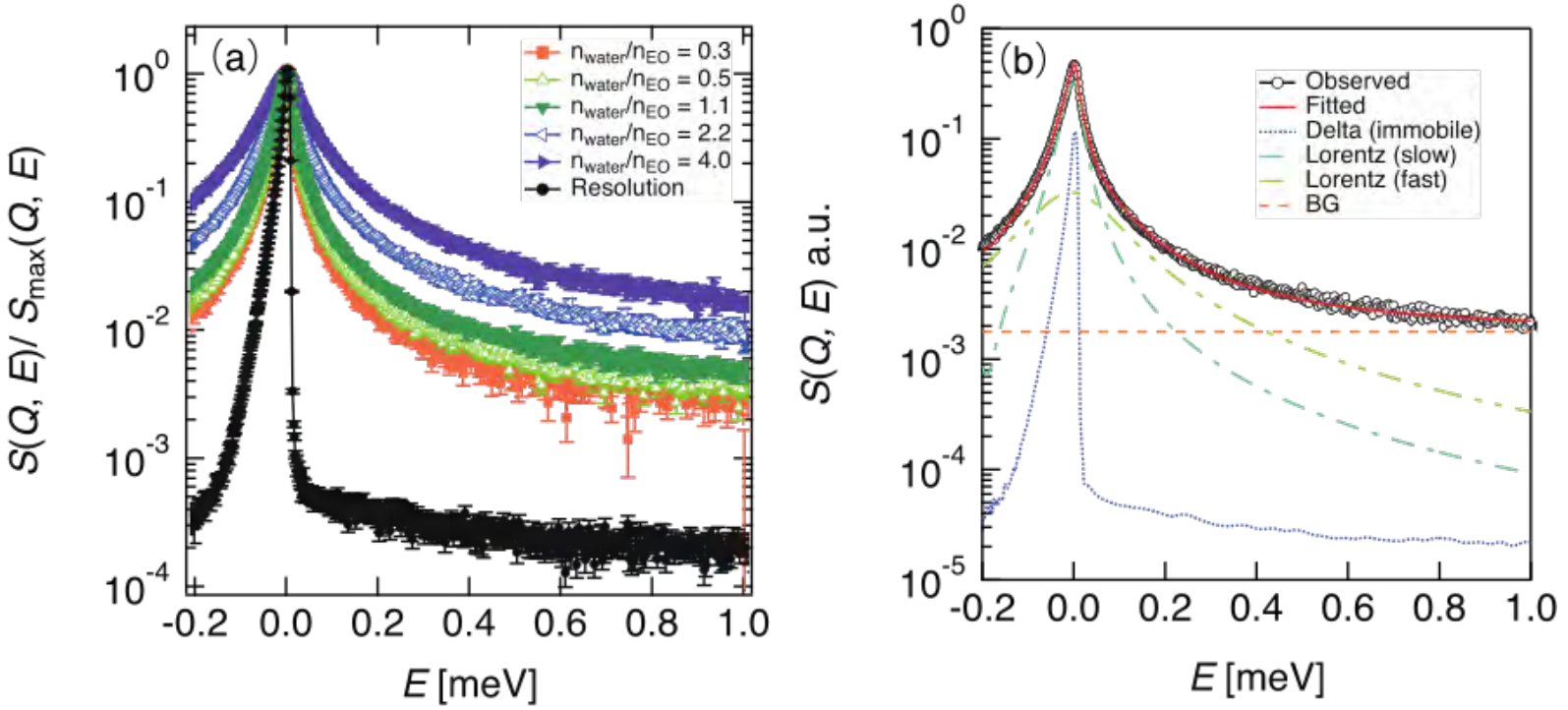
- Fourier transform from S(Q,E) to I(Q,t).
- Fitting with KWW function with β=0.5.
- Diffusion coefficients were calculated in terms of Fick's law of diffusion.

$$I(Q,t) = A_0 \exp\left[-(t/\tau_{KWW})^{\beta}\right] + (1 - A_0)$$



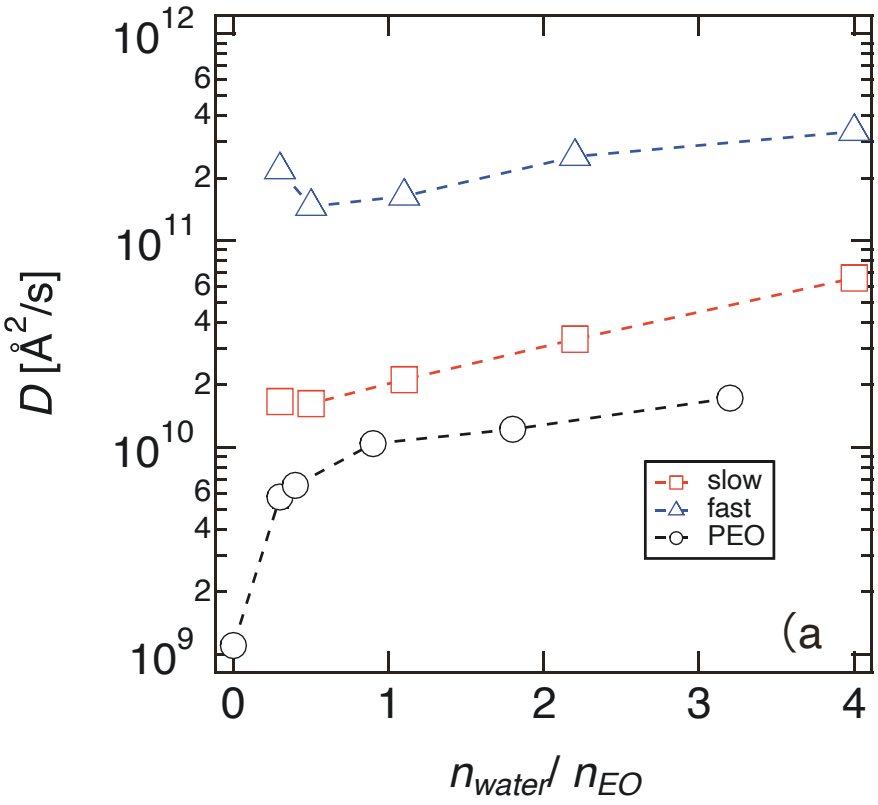
The diffusion coefficients are the order of 10^{10} Å^2/s, and increase with increasing water content.

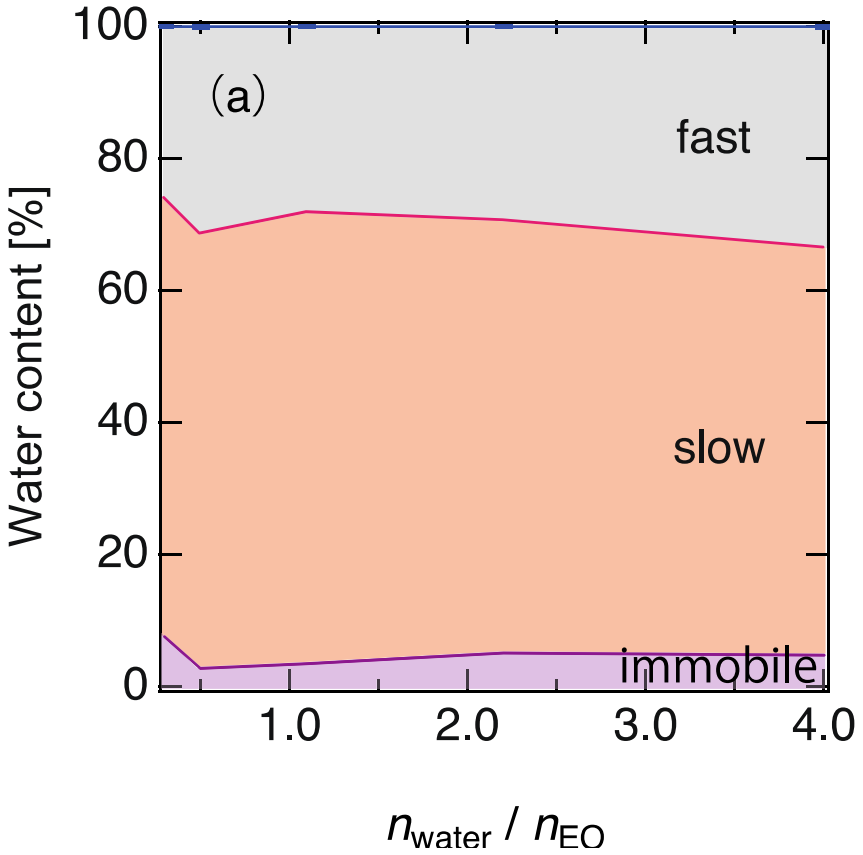
QENS of dPEO/H_2O: water motion



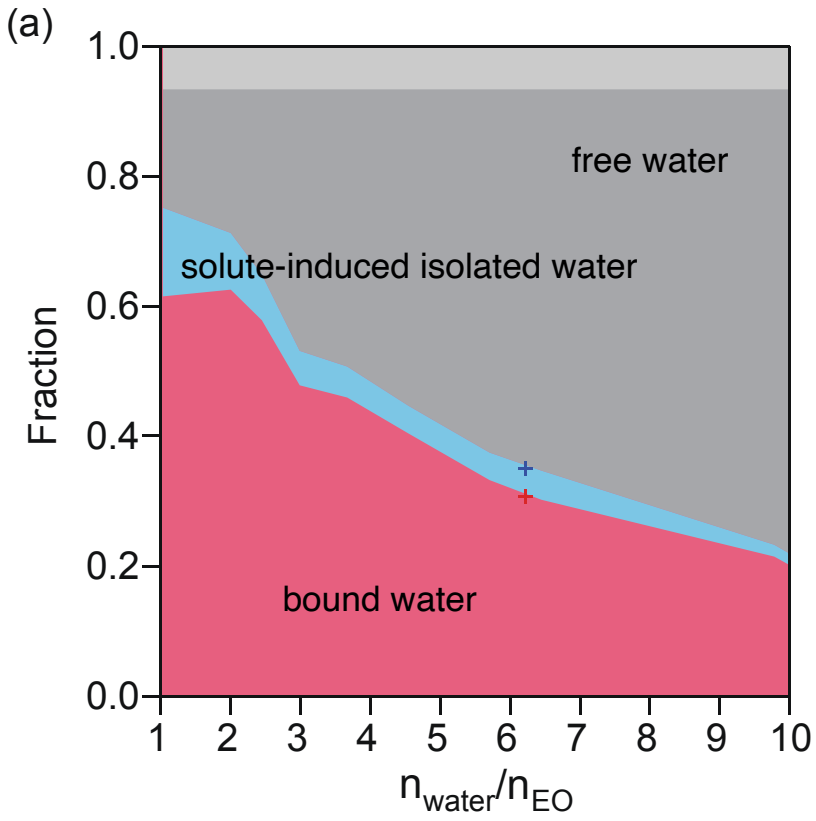
$$S(Q,E) = R(Q,E) \otimes [A_{immobile}\delta(Q,E) + A_{slow}L_{slow}(\Gamma_{slow},E) + A_{fast}L_{fast}(\Gamma_{fast},E)] + B_g$$

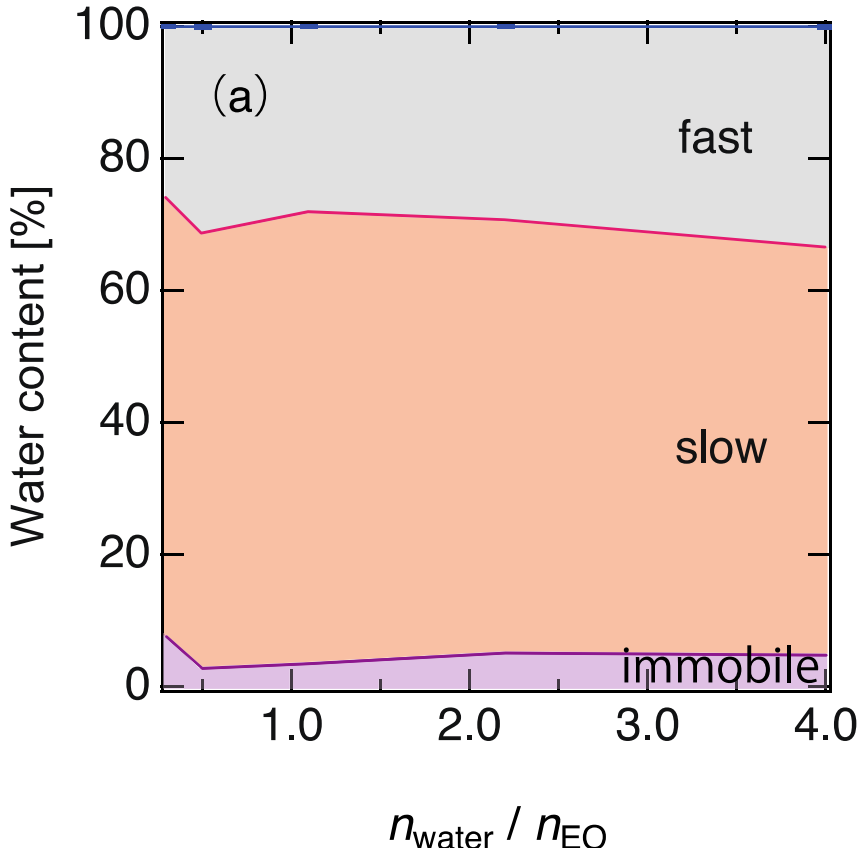
The existence of slow hydration water





Consistent with the THz-TDS results





Dynamics of PEO chains and hydration water at physiological temperature

- The existence of intermediate water is confirmed.
- Three types of water exist even at low water contents.

Q1: A detailed picture of the intermediate water?

Q2: Relation with the cold crystallization?

Data analysis of QENS profiles

Previous analysis: 3 modes (delta+2 Lorentz) were assumed.

$$S(Q,E) = R(Q,E) \otimes [A_{immobile}\delta(Q,E) + A_{slow}L_{slow}(\Gamma_{slow},E) + A_{fast}L_{fast}(\Gamma_{fast},E)] + B_g$$

Present analysis: the distribution of Lorentz functions will be calculated as an inverse problem.

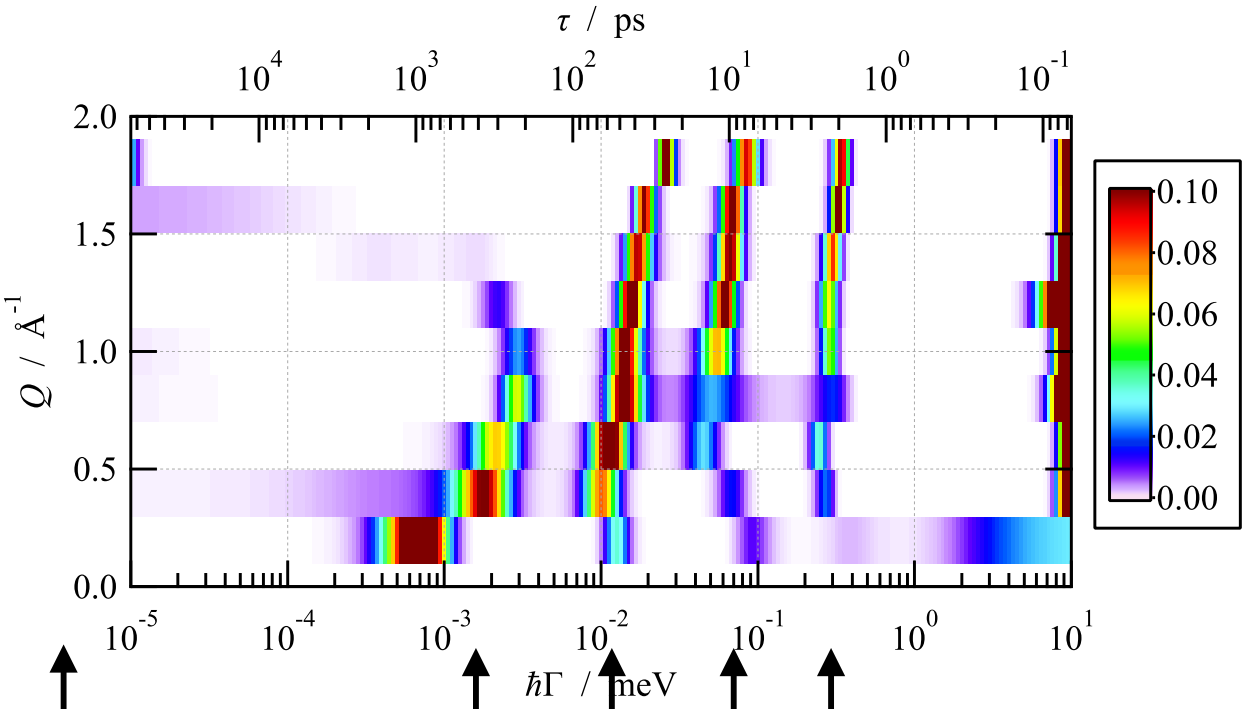
$$S(Q,E) = R(Q,E) \otimes \left[A(Q)\delta(Q,E) + \int_0^\infty B(Q,\Gamma)\frac{1}{\pi}\left(\frac{\Gamma}{\Gamma^2+E^2}\right)d\Gamma\right] + B_g$$

Mode Distribution Analysis (MDA)

T. Kikuchi et al., *Phys. Rev. E*, 2013
T. Kikuchi et al., *J. Mol. Liq.*, 2023

Mode distribution obtained by MDA

*d*PEO+30wt% H_2O (n_w/n_{EO} = 1.1), T = 310K



5)Reorientation (RO) $\hbar\Gamma \sim 3 \times 10^{-1}$ meV

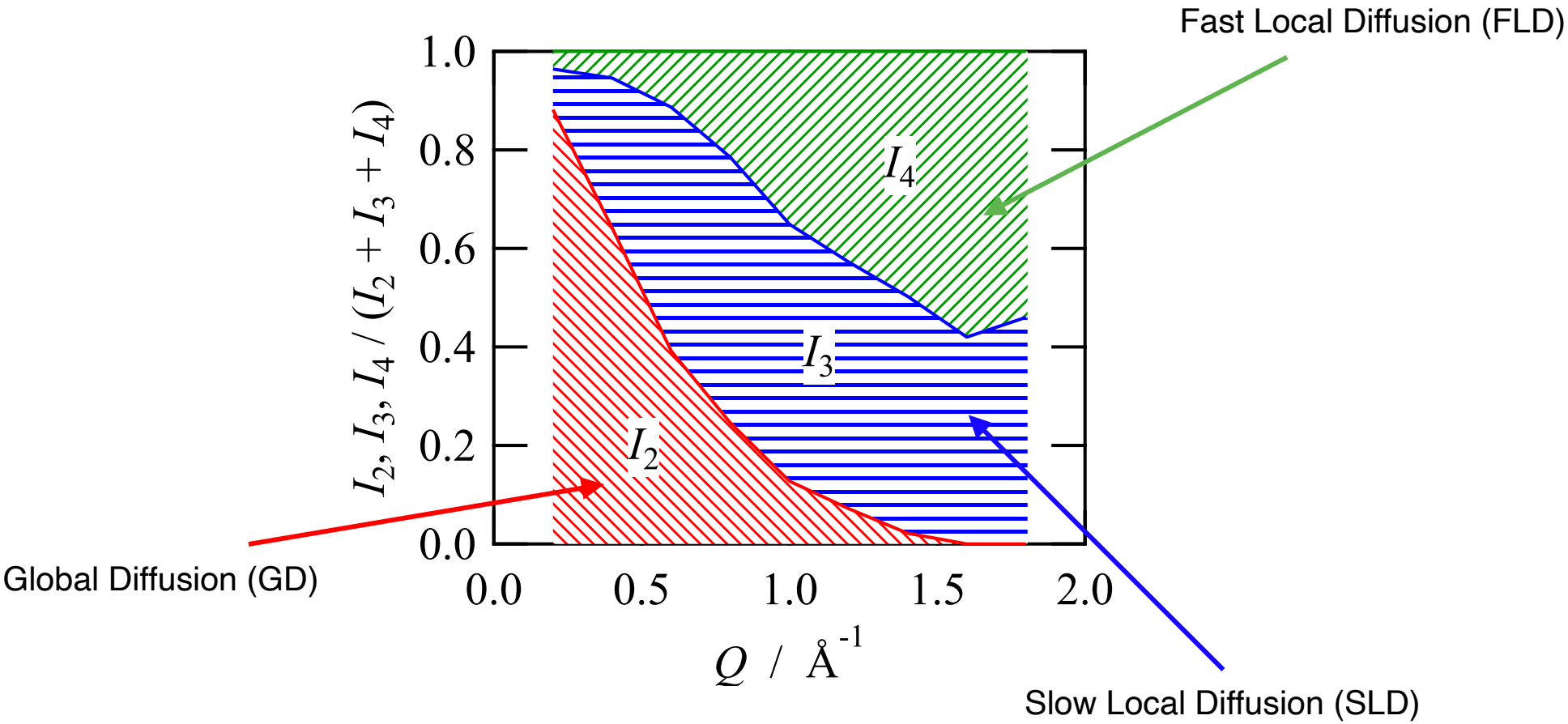
4)Fast Local Diffusion (FLD) $\hbar\Gamma \sim 10^{-1}$ meV

3)Slow Local Diffusion (SLD) $\hbar\Gamma \sim 10^{-2}$ meV

2)Global Diffusion (GD) $\hbar\Gamma \sim 10^{-3}$ meV

1)Elastic Component (EC) $\hbar\Gamma \sim 0$ meV

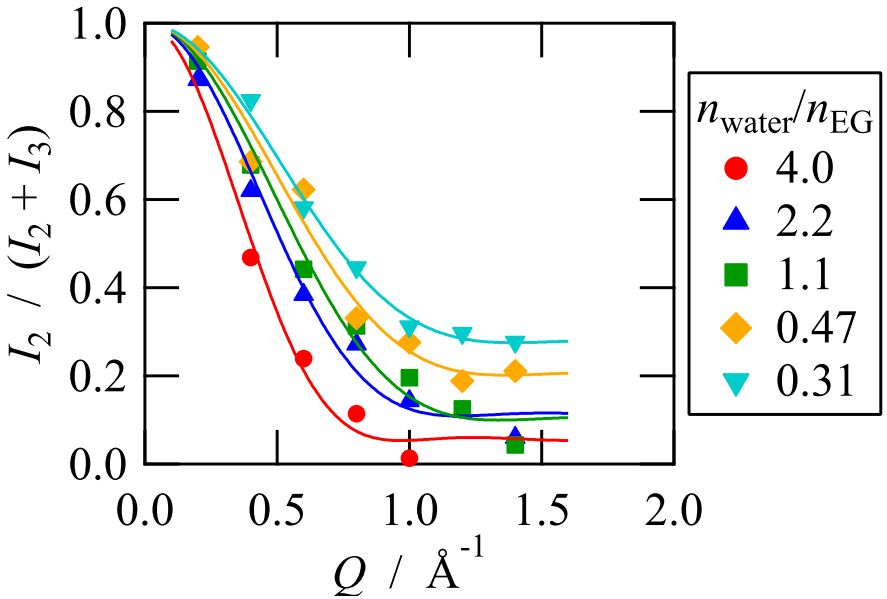
Q-dependence of the fraction of diffusive modes

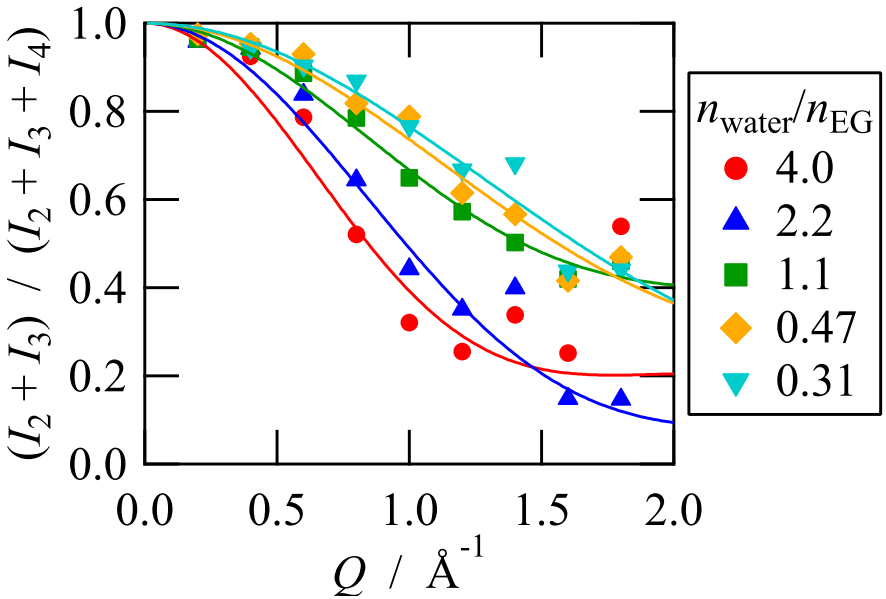


Elastic Incoherent Structure Factor

$$EISF_{SLD} = \frac{I_1}{I_1 + I_2}$$

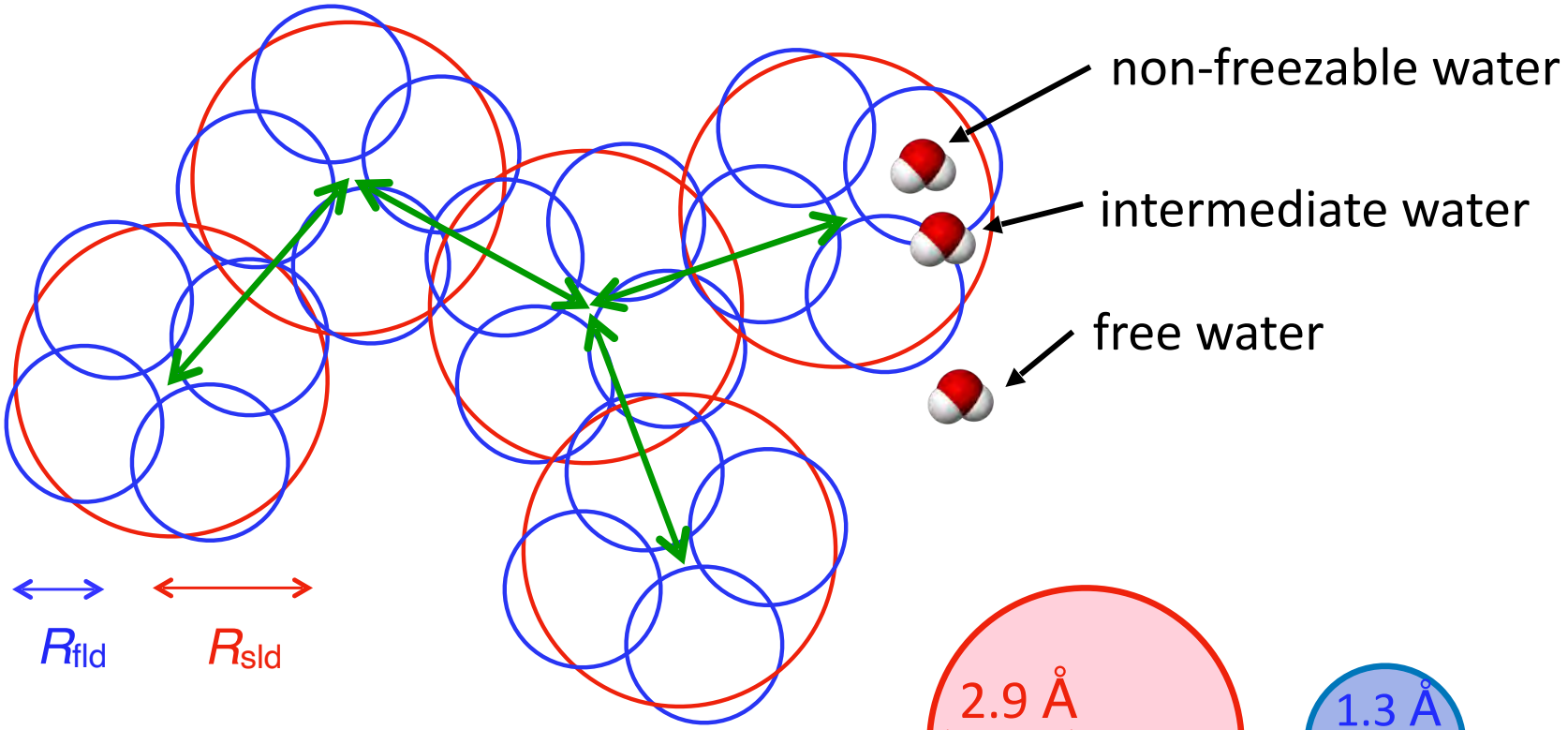
$$EISF_{FLD} = \frac{I_1 + I_2}{I_1 + I_2 + I_3}$$

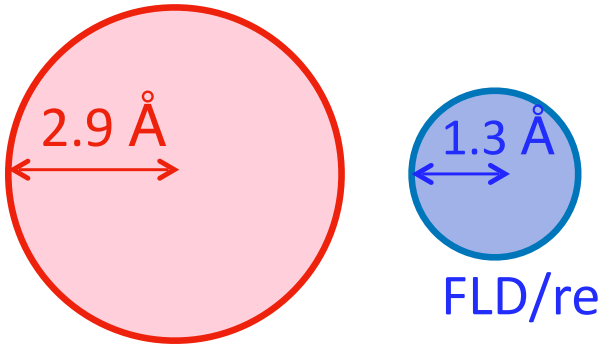




$$I(Q) = (1 - y_0)\left[\frac{3j_1^2(QR)}{QR}\right]^2 + y_0$$

Detailed picture of the hydration water





FLD/relaxation time:10 ps

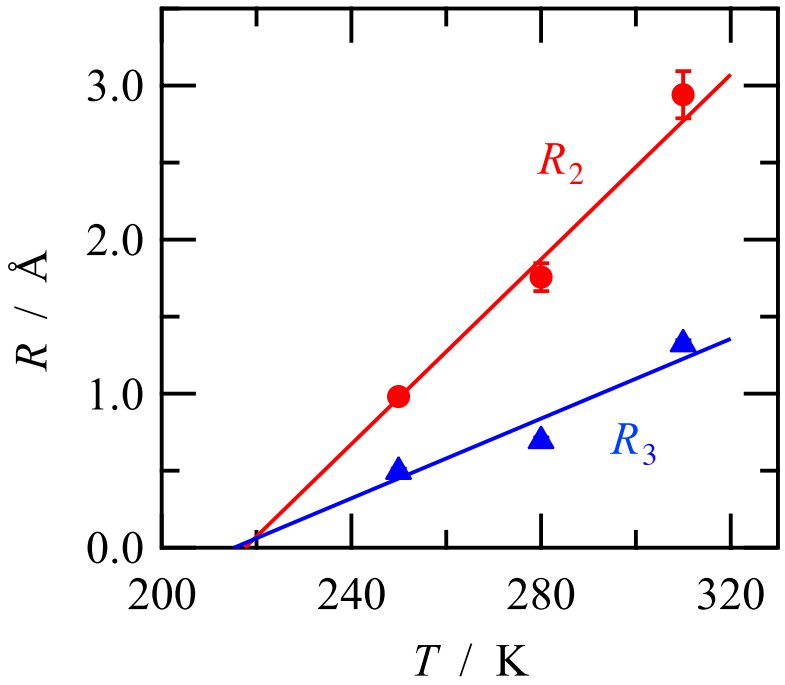
GD/ jump distance: 4.8 Å
mean residence time: 130 ps

SLD/ relaxation time: 41 ps

Temperature dependence of R_2, R_3

T. Kikuchi, et al., *J. Chem. Phys.*, 2024

The cage sizes monotonically decreased with decreasing temperature.



Hydration water molecules stop moving at 220-250K.

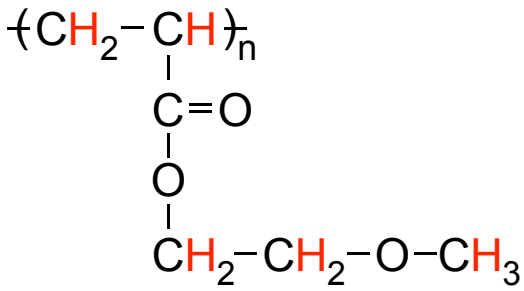
The cold crystallization occurs on heating around T=250 K.

QENS experiments on PMEA and water

PMEA: poly(2-methoxyethyl acrylate)

- excellent biocompatibility: the largest market share in the world
  - low protein adhesion and denaturation
  - low blood cells adhesion and activation
  - low toxicity
- water insoluble

<u>*h*PMEA+D_2O</u>

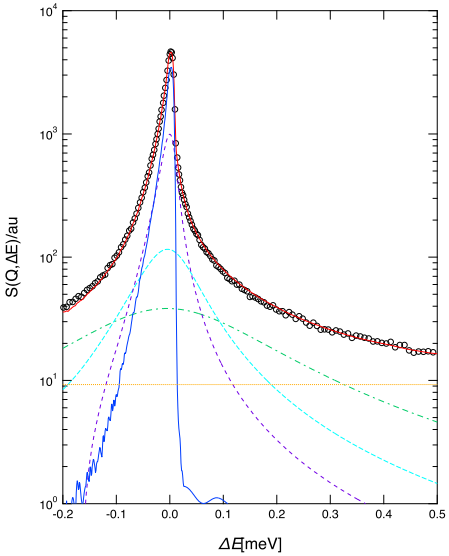


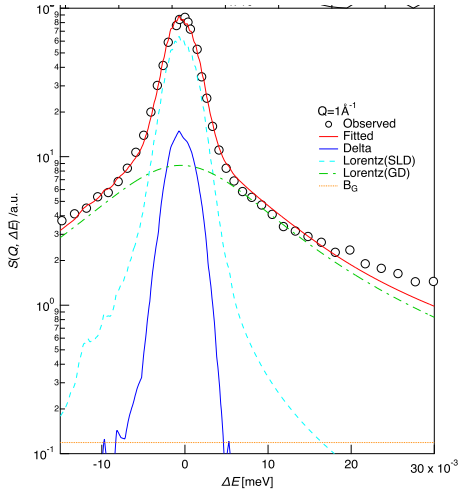
D_2O

<u>*d*PMEA+H_2O</u>

H_2O

*d*PMEA/H_2O: water motion





High-Flux mode

E_{reso} = 12 μeV

-40 < ΔE < 1000 μeV

$$S(Q,E) = R(Q,E) \otimes [A_{HF0}(Q)\delta(Q,E) + A_{HF1}(Q)L(\Gamma_{HF1}(Q),E) + A_{HF2}(Q)L(\Gamma_{HF2}(Q),E) + A_{HF3}(Q)L(\Gamma_{HF3}(Q),E)] + B_g(Q)$$

High-Resolution mode

E_{reso} = 3.6 μeV

-20 < ΔE < 50 μeV

$$S(Q,E) = R(Q,E) \otimes [A_{HR0}(Q)\delta(Q,E) + A_{HR1}(Q)L(\Gamma_{HR1}(Q),E) + A_{HR2}(Q)L(\Gamma_{HR2}(Q),E)] + B_g(Q)$$

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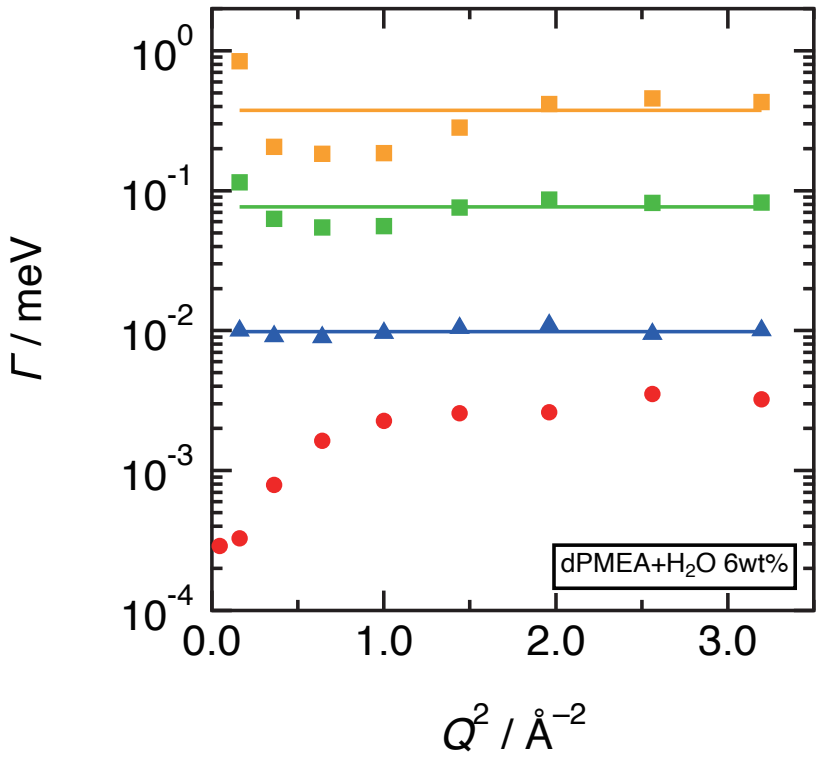
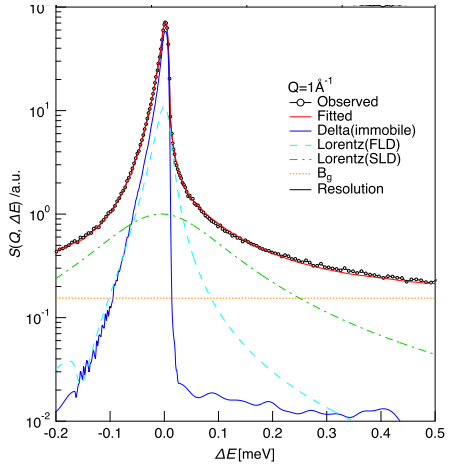
4 modes in water motion



$\hbar\Gamma \sim 3 \times 10^{-1}$ meV	Reorientation (RO)
$\hbar\Gamma \sim 10^{-1}$ meV	Fast Local Diffusion (FLD)
$\hbar\Gamma \sim 10^{-2}$ meV	Slow Local Diffusion (SLD)
$\hbar\Gamma \sim 10^{-3}$ meV	Global Diffusion (GD)

Almost the same as the case of PEO hydration water.

*h*PMEA/D_2O: polymer motion

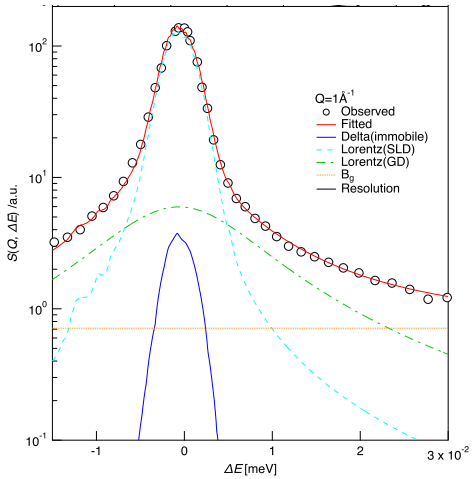


High-Flux mode

E_{reso} = 12 μeV

-40 < ΔE < 1000 μeV

$$S(Q,E) = R(Q,E) \otimes [A_{HF0}(Q)\delta(Q,E) + A_{HF1}(Q)L(\Gamma_{HF1}(Q),E) + A_{HF2}(Q)L(\Gamma_{HF2}(Q),E)] + B_g(Q)$$



High-Resolution mode

E_{reso} = 3.6 μeV

-20 < ΔE < 50 μeV

$$S(Q,E) = R(Q,E) \otimes [A_{HR0}(Q)\delta(Q,E) + A_{HR1}(Q)L(\Gamma_{HR1}(Q),E) + A_{HR2}(Q)L(\Gamma_{HR2}(Q),E)] + B_g(Q)$$

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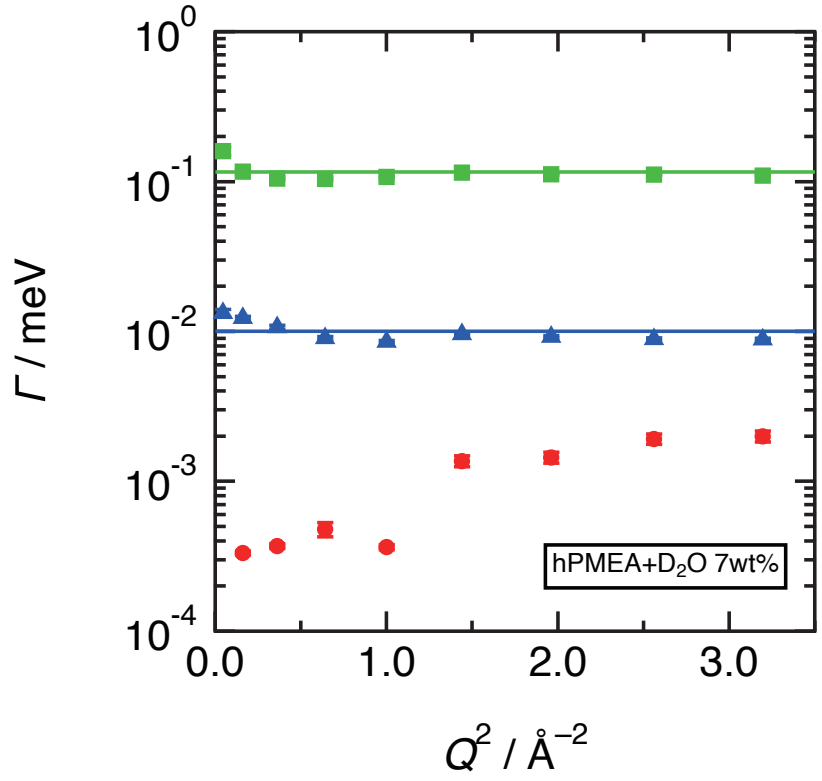
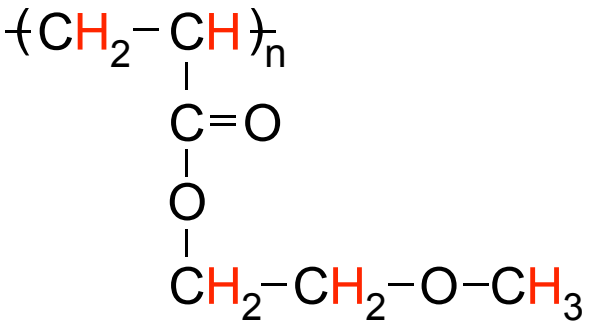
3 modes in polymer motion



$\hbar\Gamma \sim 10^{-1}\,\mathrm{meV}$ Fast Local Diffusion (FLD)

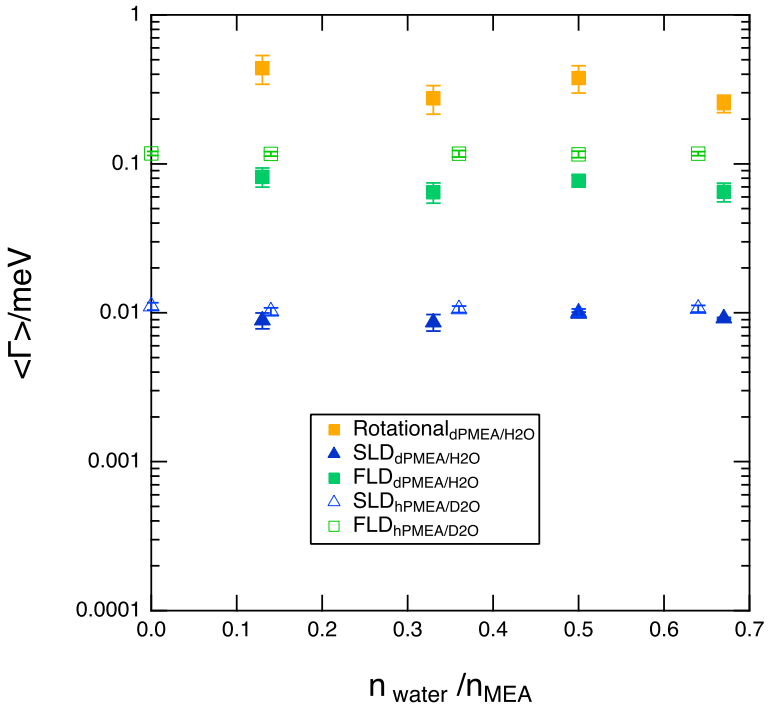
$\hbar\Gamma \sim 10^{-2}\,\mathrm{meV}$ Slow Local Diffusion (SLD)

$\hbar\Gamma \sim 10^{-3}\,\mathrm{meV}$ Global Diffusion (GD)



Similar behavior to the water dynamics.

Relation between water and polymer motions

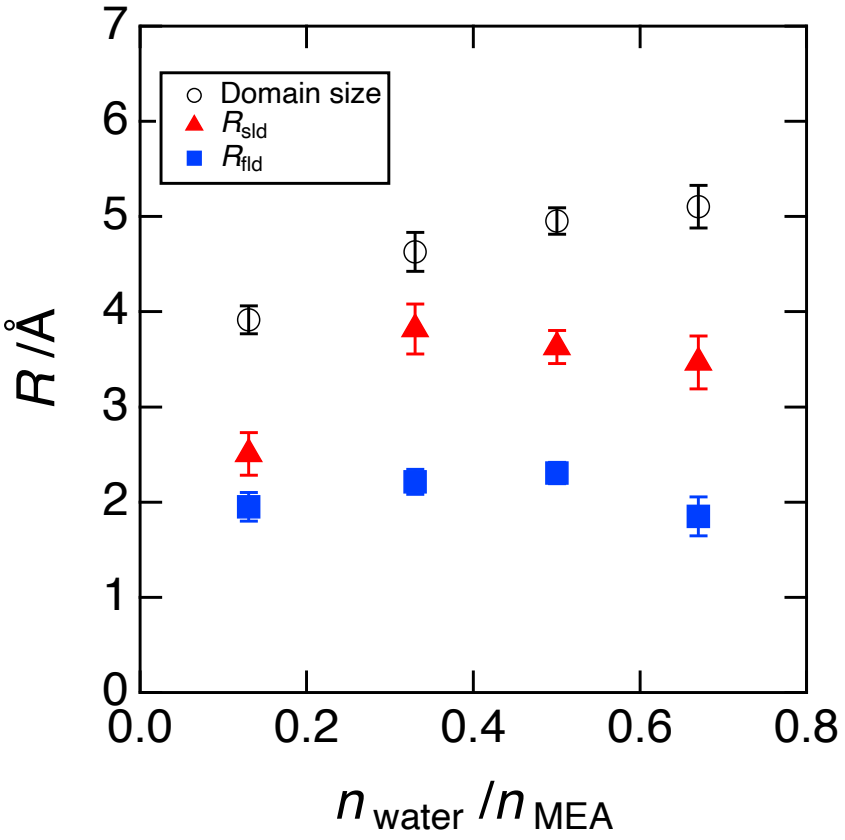


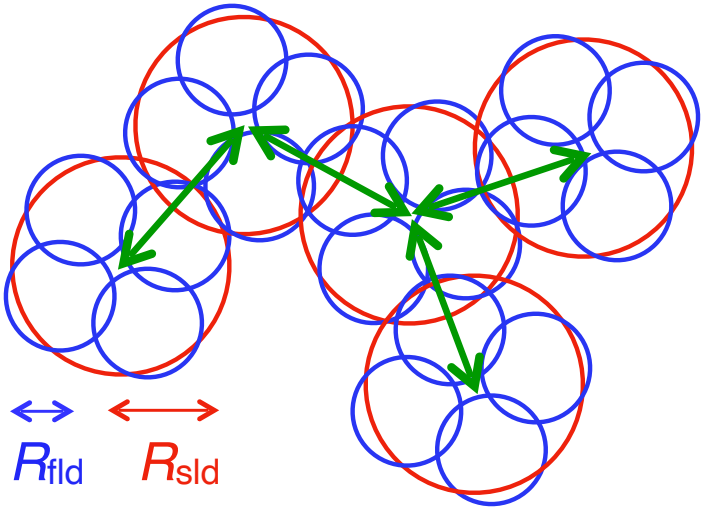
$\hbar\Gamma \sim 3 \times 10^{-1}$ meV Reorientation (RO)

$\hbar\Gamma \sim 10^{-1}$ meV Fast Local Diffusion (FLD)

$\hbar\Gamma \sim 10^{-2}$ meV Slow Local Diffusion (SLD)

SLD and FLD of water molecules





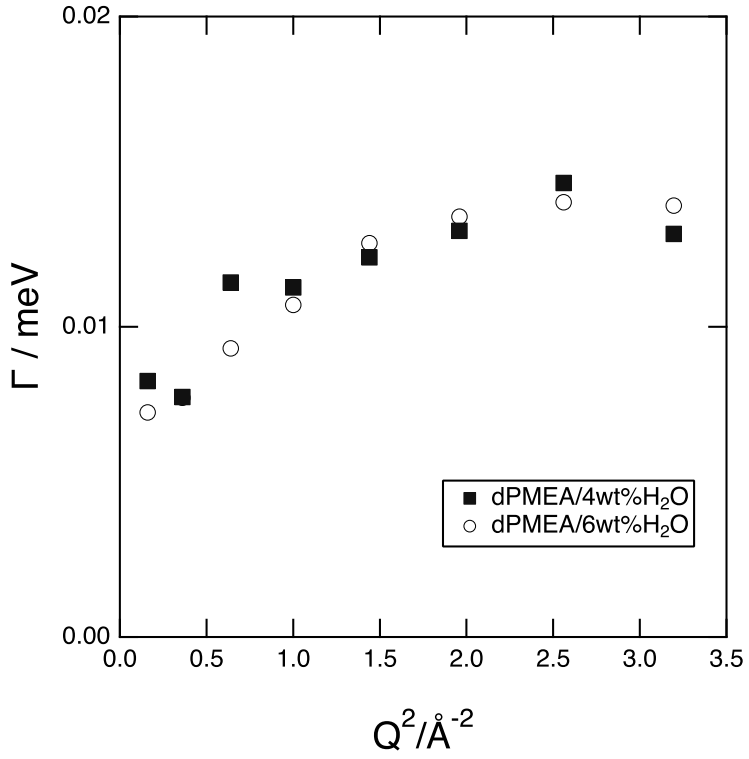
Cf. Hydration water at PEO

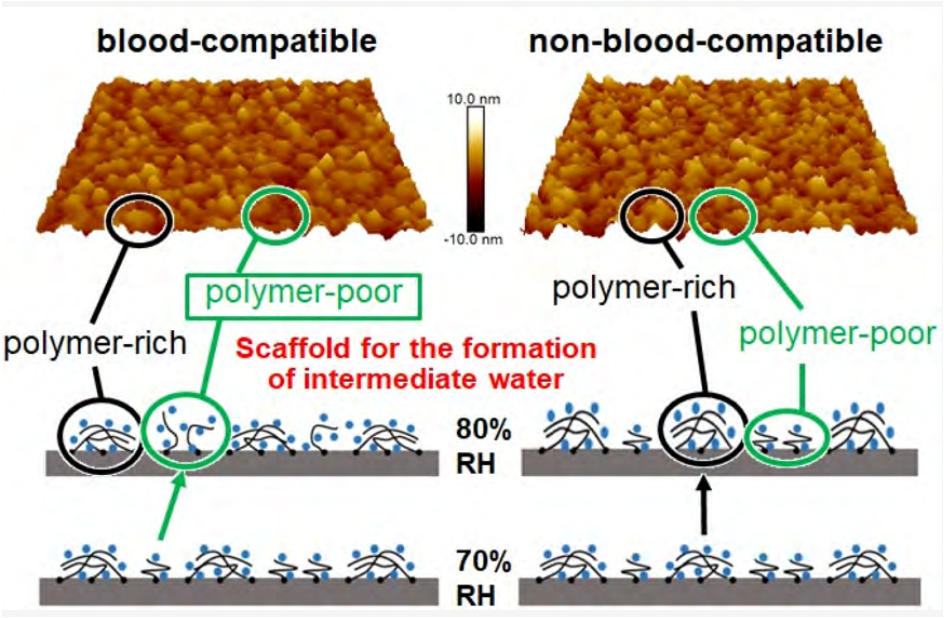
R_{sld} = 2.9 Å

R_{fld} = 1.3 Å

D_{gd} = 4.8 Å

Domain structure may be important





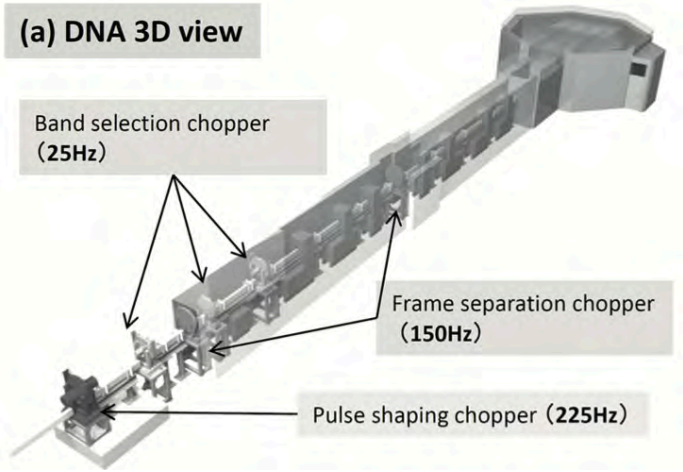
Murakami et al., Langmuir, 2022

Summary

- We have investigated the dynamics of hydration water of lipid bilayers and biocompatible polymers by QENS. These results indicated that the dynamics of hydration water is slowed down by the interaction with biocompatible materials, which suggested that the existence of the intermediate water.
- By MDA, a detailed picture of the hydration water is given.
- The origin of the cold crystallization is proposed.
- Hydration water dynamics at PMEA is similar to that at PEO, however, the difference was observed.

Collaborators

- T. Tominaga, T. Yamada (CROSS)
- T. Kikuchi (KEK/Sumitomo Rubber Ind.)
- D. Murakami (Kindai U.)
- M. Tanaka (Kyushu U.)
- M. Hishida, S. Shiomoto (Tokyo Science U.)



QENS exps. at DNA in J-PARC

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Aquatic Functional Materials