Recent Topics

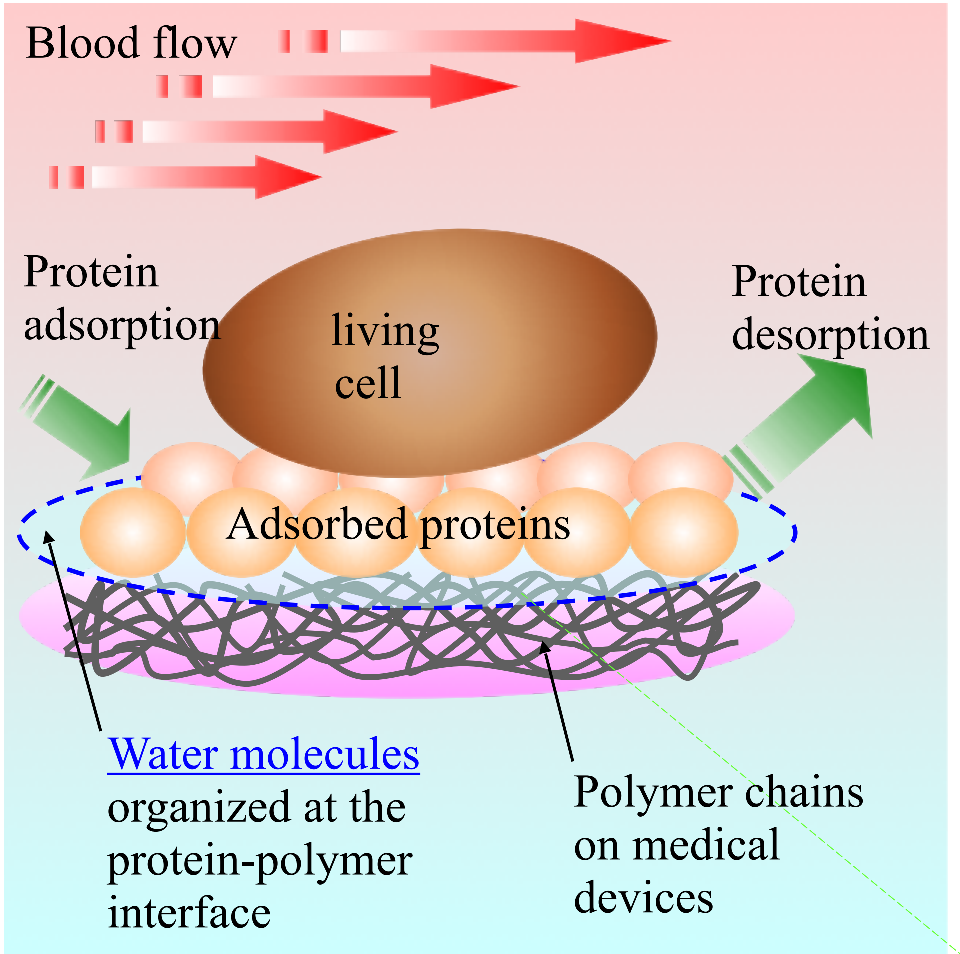
生体親和性高分子の水和水

KEK物構研

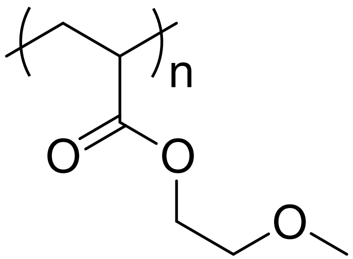
瀬戸秀紀

Biocompatible polymers

- Essentially important for biomedical devices
  - blood-contacting medical devices such as artificial organs and drug delivery carriers
- Prevent thrombus formation
  - development of biocompatible polymers: inhibit the protein adhesion / denaturation behavior at the surface of the polymer materials



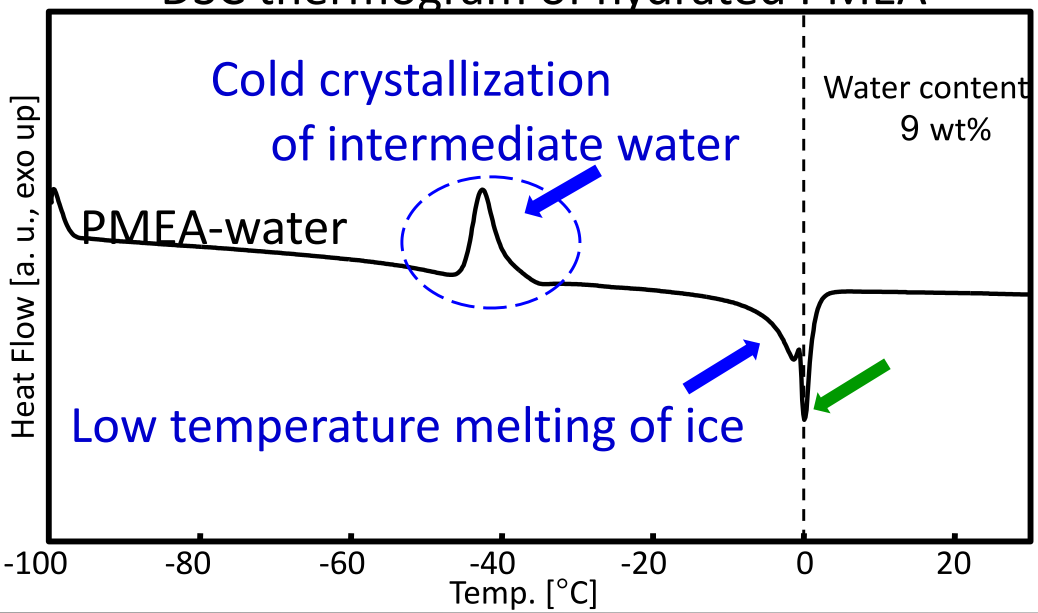
The most popular biocompatible polymer



PMEA
poly(2-methoxyethyl acrylate)

- The largest market share in the world (artificial lung)
- Excellent blood compatibility (compliment, coagulation, etc.)
- Water insoluble
- Low protein adhesion and denaturation
- Low blood cells adhesion and activation
- Low toxicity, approved by FDA

DSC thermogram of hydrated PMEA



free Water
Melting at 0 °C

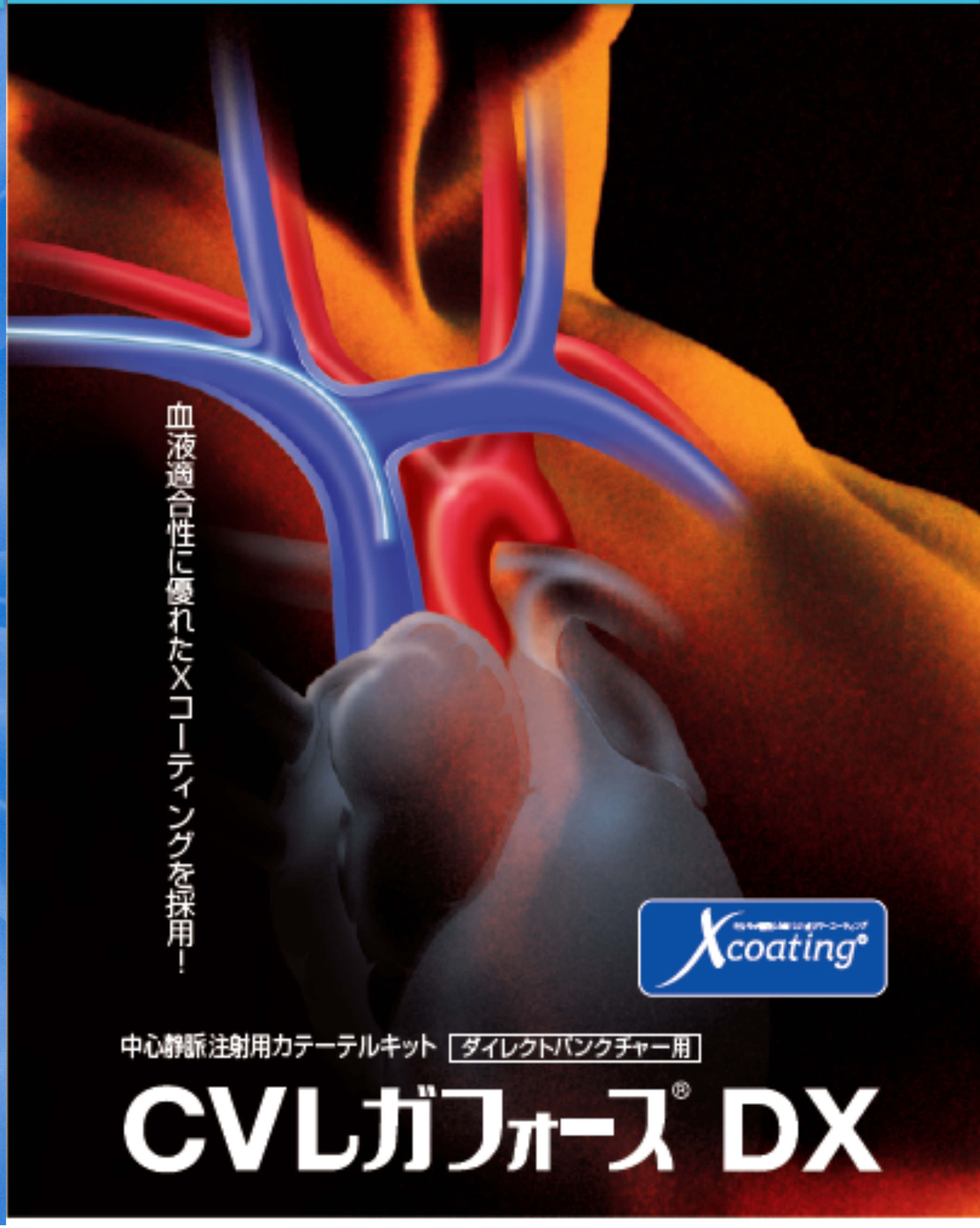
intermediate Water
Crystallizes below 0 °C

non-Freezing Water
Not crystallizes even at -100 °C

M. Tanaka *et al*., *Biomaterials*, 2000.
M. Tanaka *et al*., JP Patent 4746987.

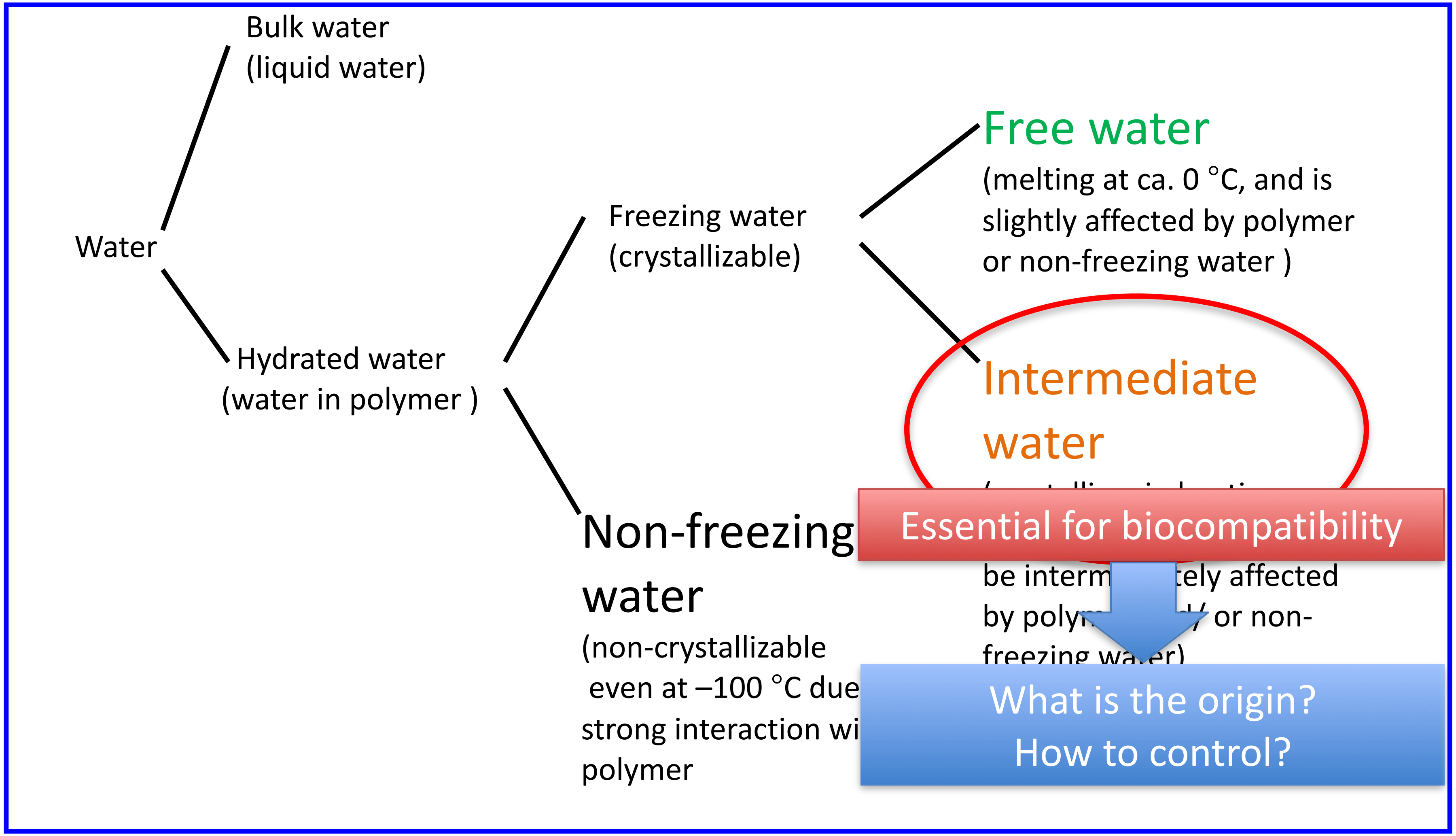
Artificial lung & heart

Artificial blood vessel & Catheter



Classification of water

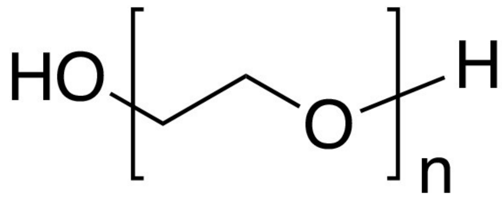
*from DSC, IR, and NMR



Polyethylene Oxide(PEO)/water

T. Tominaga, HS et al., 2022

PEO (polyethylene oxide)
- ✓ water: good solvent
- ✓ typical biocompatible polymer
- ✓ deuterated PEO is commercially available
- ✓ “Cold Crystallization” depends on water content



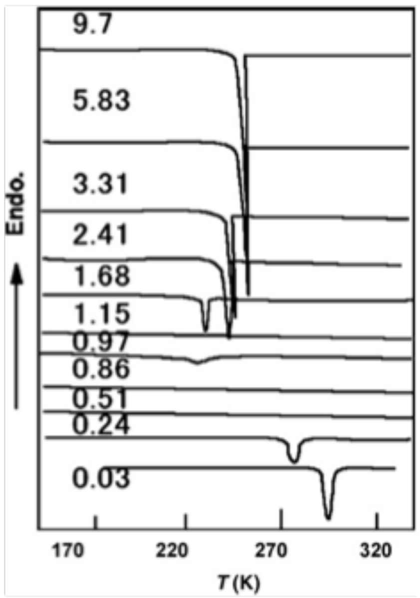


Fig. 1. DSC cooling curves of PEG–water systems. Numerals in the figure show water content (W_c) in g g^{-1} and cooling rate = 10 K min^{-1}.

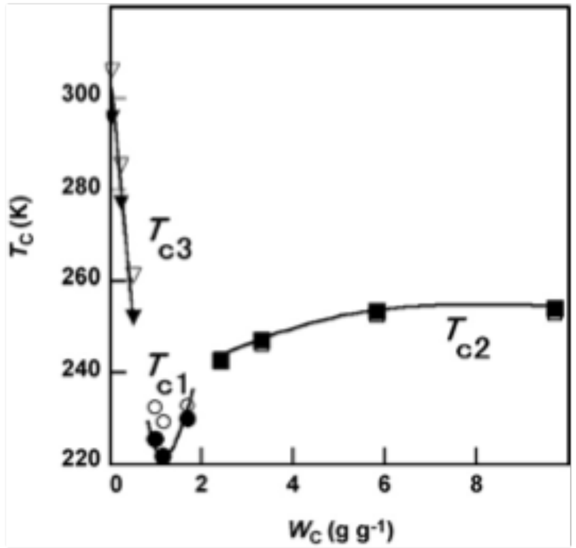


Fig. 2. Relationships between crystallization temperatures and water content. (●) Crystallization categorized into group 1; (■) group 2; (▼) group 3.

O-O distance in PEO vs hydrogen bonding of water network

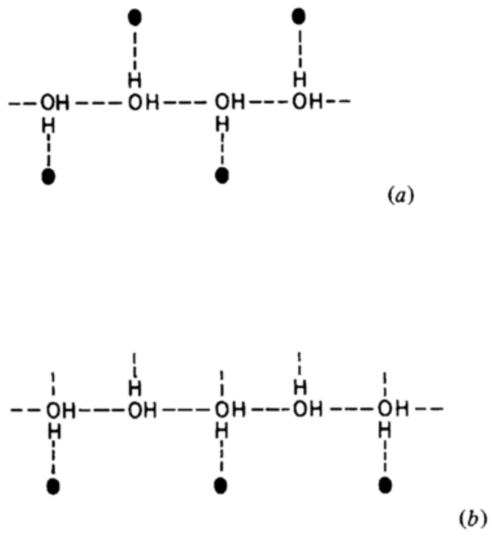


FIG. 1.—Simplified picture showing the difference between possible linking of the water molecules bound to PEO in the cases (*a*) $n_w = 1$ and (*b*) $n_w = 2$. At $n_w = 1$ there are no hydrogen atoms available to form a *cross-linked* system of water chains as required, while this can be accomplished at $n_w = 2$ (shown with the broken lines to the imagined neighbouring water chains). (----) Hydrogen bond, (●) ether oxygen.

J. Chem. SOC, Faraday Trans.1, 1981, 77, 2053-2077

The number ratio of EO and H_2O (n_{water}/ n_{EO}) is important for the formation of water network.

TABLE 1.—SOLUBILITY OF SOME POLYETHERS IN WATER

polymer	formula	soluble (s)/ insoluble (i) in water
poly(methylene oxide); (PMO)	$(-O-CH_2-)_m$	i
poly(acetaldehyde)	$(-O-CH(CH_3)-)_m$	i
poly(ethylene oxide); (PEO)	$(-O-CH_2-CH_2-)_m$	s
poly(propylene oxide); (PPO)	$(-O-CH_2-CH(CH_3)-)_m$	i
poly(trimethylene oxide)	$(-O-CH_2-CH_2-CH_2-)_m$	i
poly(tetrahydrofuran)	$[-O-(CH_2)_4-]_m$	i

IMSS 物質構造科学研究所

Aquatic Functional Materials

Sample preparation

Dynamic behavior of water molecules: dPEO/H_2O

Molecular weight of dPEO: 17,000 g/mol

Molecular weight distribution: 1.07 (Polymer Source Inc.)

Dynamic behavior of polymer chains: hPEO/D_2O

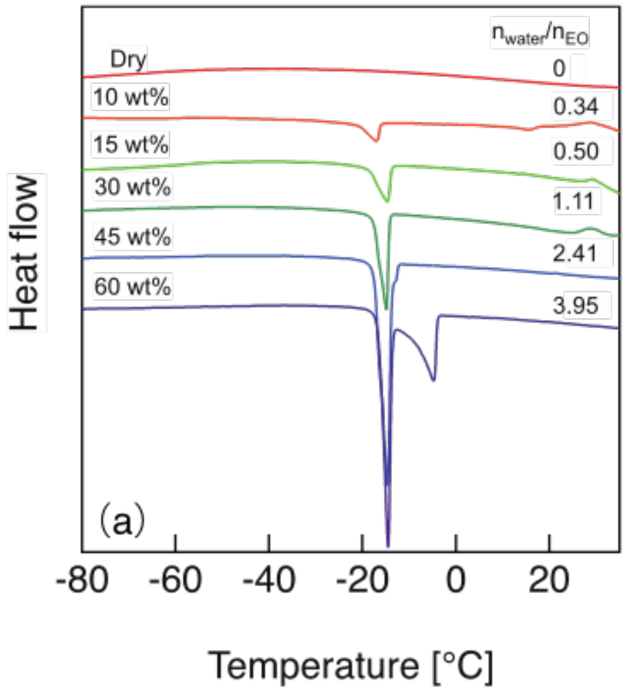
Molecular weight of hPEO: 16,000 g/mol

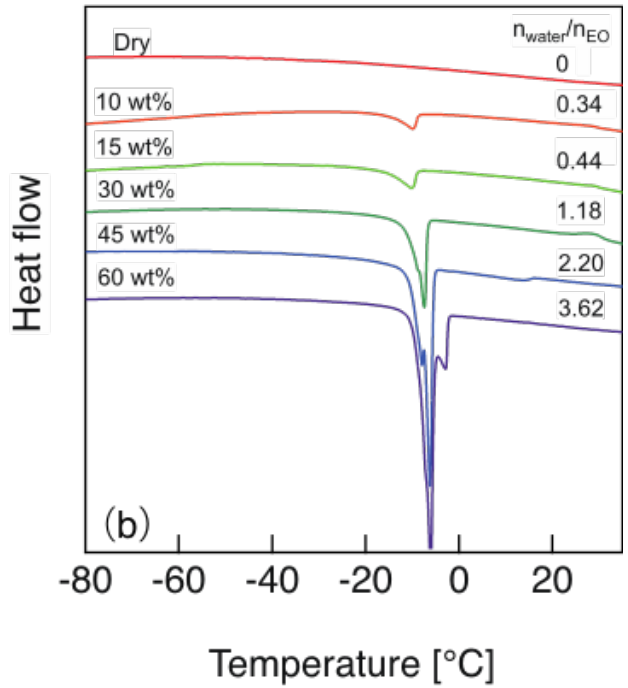
Molecular weight distribution: 1.05 (Polymer Source Inc.)

Table S1: Samples for QENS and DSC with their water contents.

Sample Name	Water Contents (wt%) $\langle n_{water}/n_{EO} \rangle$	
	QENS samples	DSC samples
*d*PEO(dry)	N/A	0.0 ⟨0.0⟩
*d*PEO/H_2O(10 wt%)	10.3 ⟨0.3⟩	11.5 ⟨0.35⟩
*d*PEO/H_2O(15 wt%)	15.0 ⟨0.5⟩	15.1 ⟨0.47⟩
*d*PEO/H_2O(30 wt%)	29.9 ⟨1.1⟩	30.5 ⟨1.17⟩
*d*PEO/H_2O(45 wt%)	45.3 ⟨2.2⟩	42.5 ⟨1.97⟩
*d*PEO/H_2O(60 wt%)	59.8 ⟨4.0⟩	58.8 ⟨3.81⟩
*h*PEO(dry)	0.0 ⟨0.0⟩	0.0 ⟨0.0⟩
*h*PEO/D_2O(10 wt%)	10.9 ⟨0.3⟩	10.2 ⟨0.25⟩
*h*PEO/D_2O(15 wt%)	15.0 ⟨0.4⟩	14.5 ⟨0.37⟩
*h*PEO/D_2O(30 wt%)	29.9 ⟨0.9⟩	30.3 ⟨0.96⟩
*h*PEO/D_2O(45 wt%)	44.9 ⟨1.8⟩	48.6 ⟨2.08⟩
*h*PEO/D_2O(60 wt%)	59.4 ⟨3.2⟩	62.0 ⟨3.59⟩

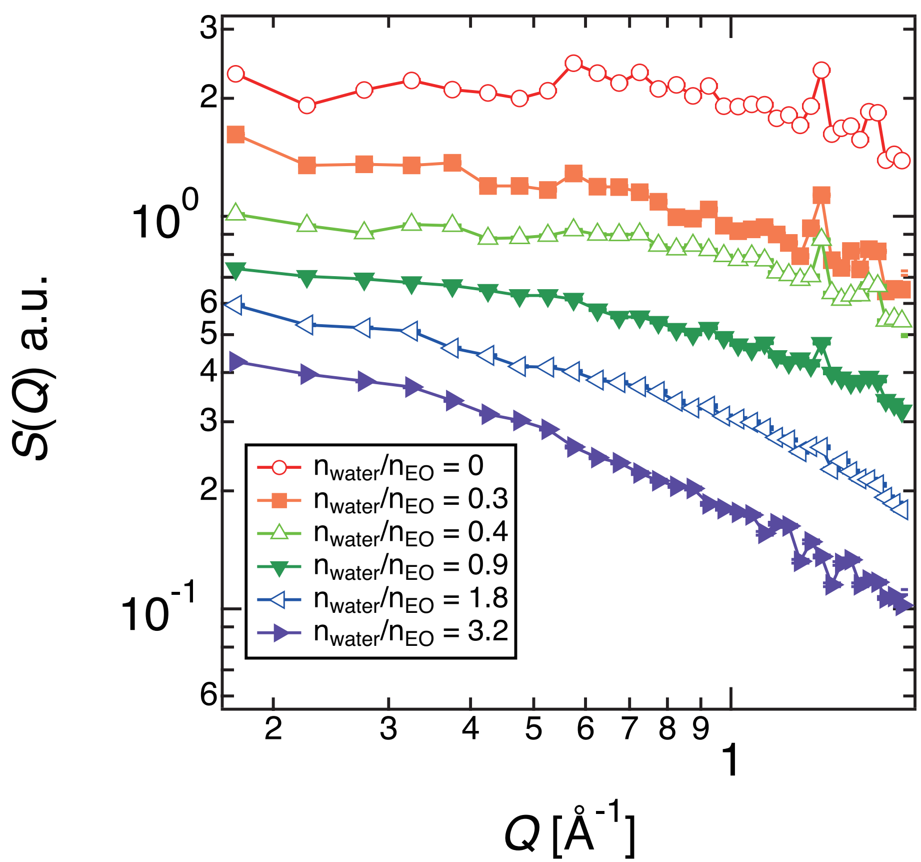
DSC measurements





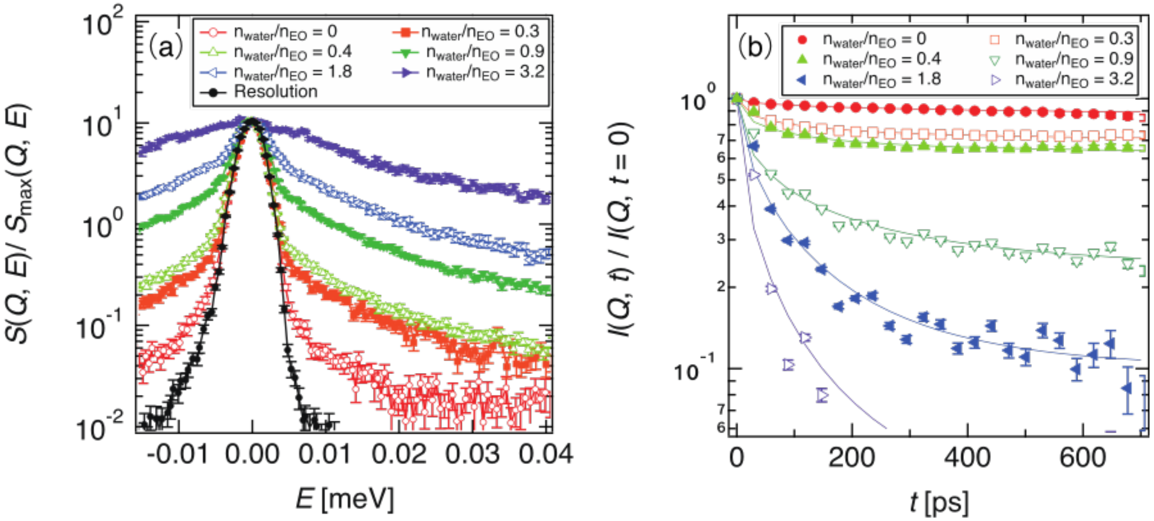
DSC curves of (a) *d*PEO/H_2O and (b) *h*PEO/D_2O.

S(Q) of hPEO/D_2O



Elastic scattering intensity $S(Q)$ for the *h*PEO-D_2O samples at each n_{water}/n_{EO} ratios. The profiles are shifted appropriately for better visualization. These profiles were obtained by the integration of $S(Q, E)$ at $20 < E < 100$ (μeV) under $0.125 < Q < 1.875$ $Å^{-1}$

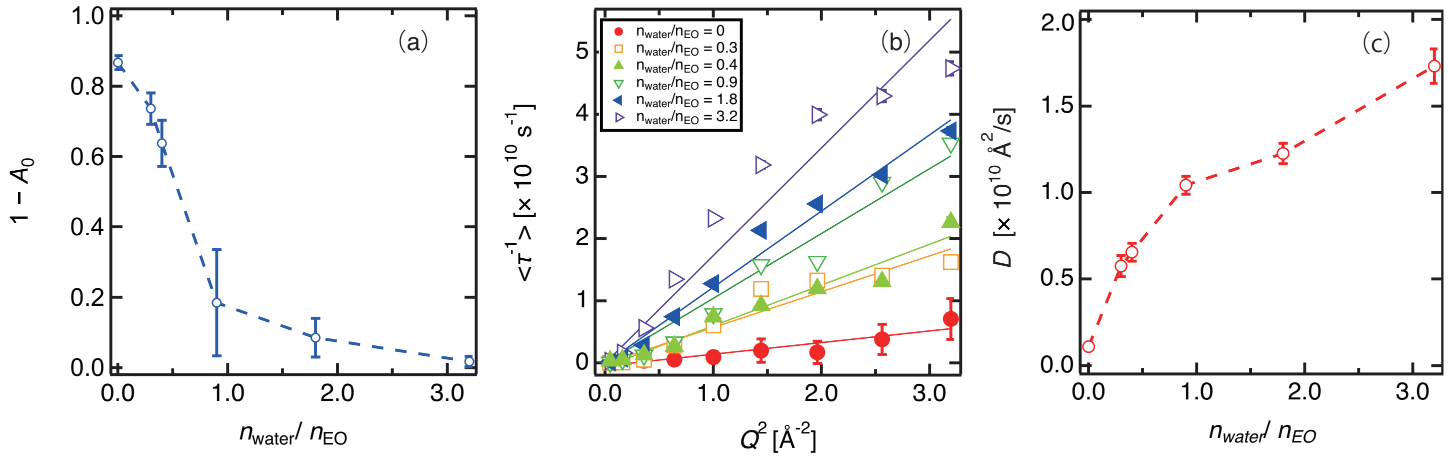
QENS of hPEO/D_2O



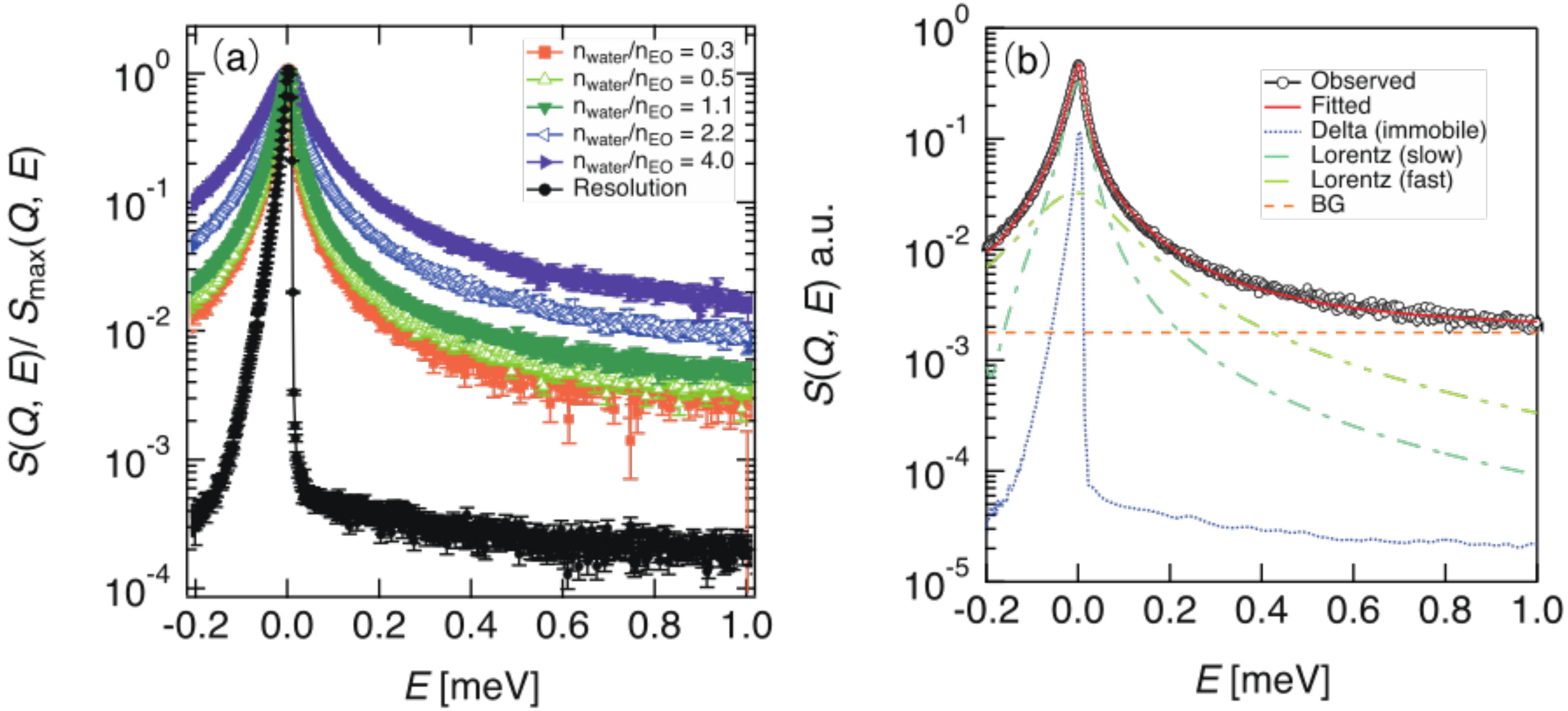
- Fourier transform from S(Q,E) to I(Q,t).
- Fitting with KWW function with β=0.5.
- Diffusion coefficients were calculated in terms of Fick's law of diffusion.

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

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

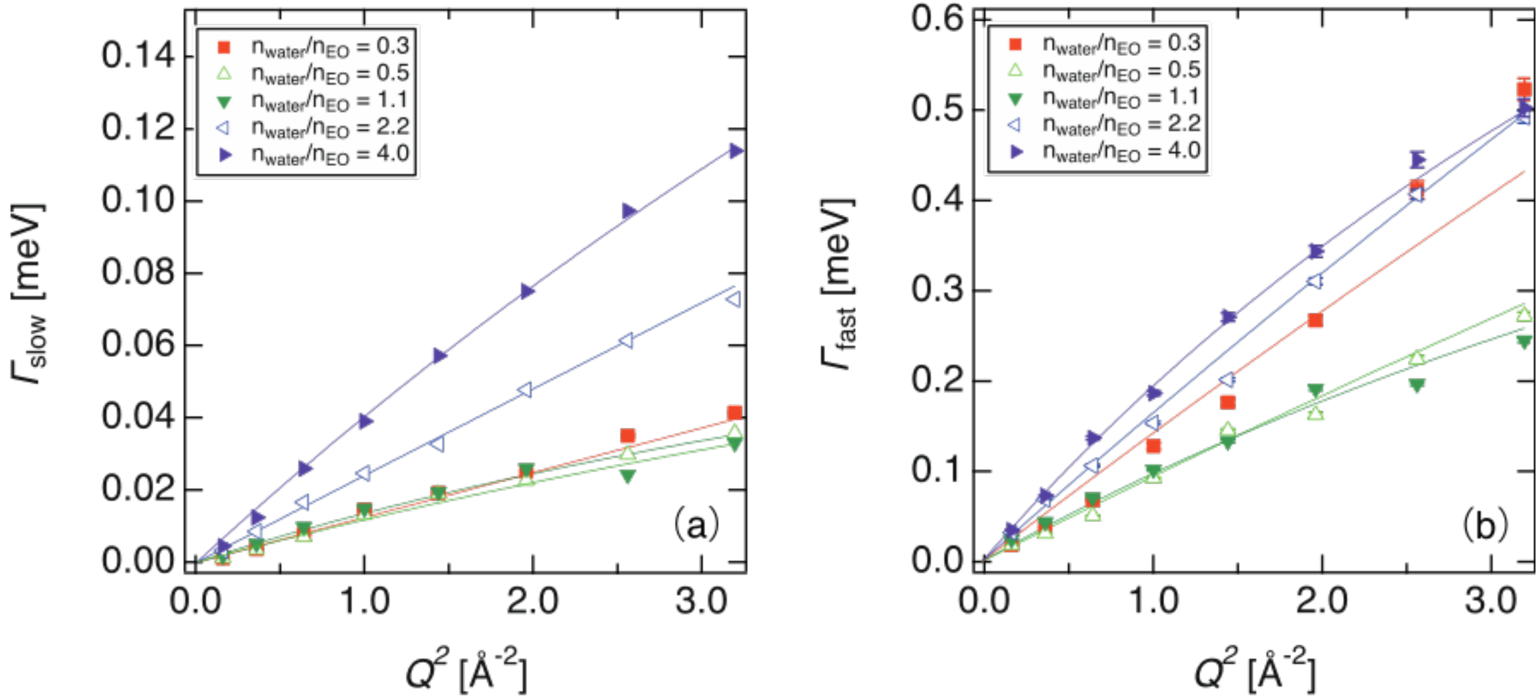


QENS of dPEO/H_2O



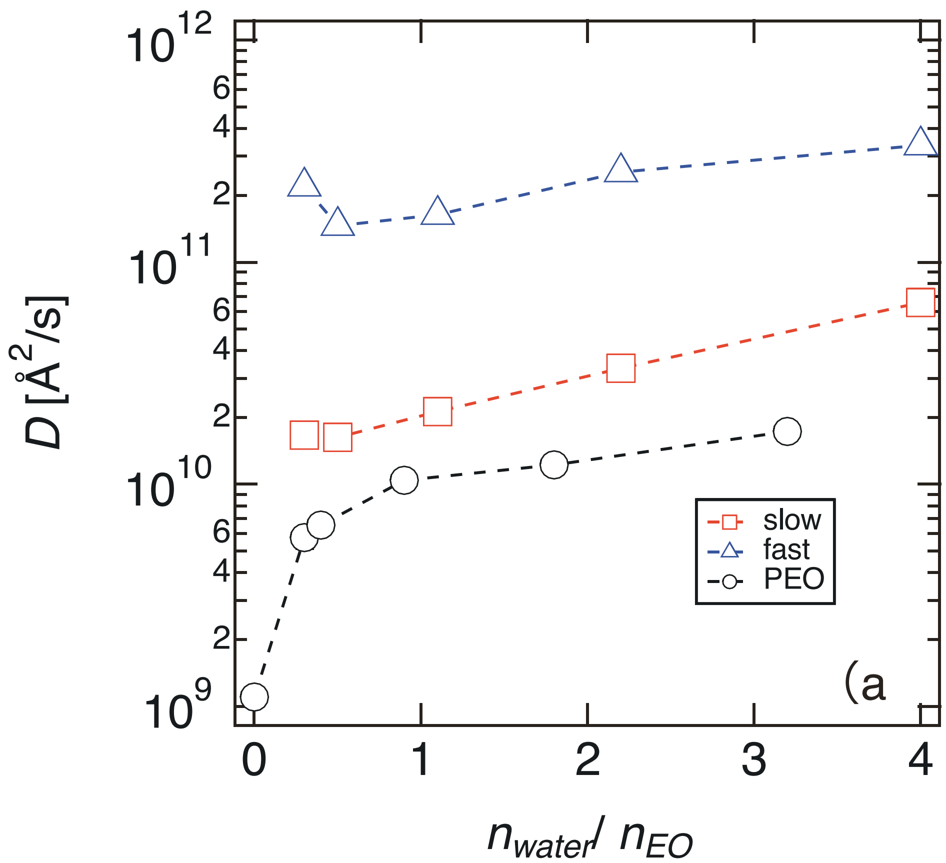
$$S(Q,E) = R(Q,E) \otimes [A_{immobile}\delta(Q,E) + A_{slow}L_{slow}(\Gamma_{slow},E) + A_{fast}L_{fast}(\Gamma_{fast},E)] + B_g$$

Jump Diffusion Model



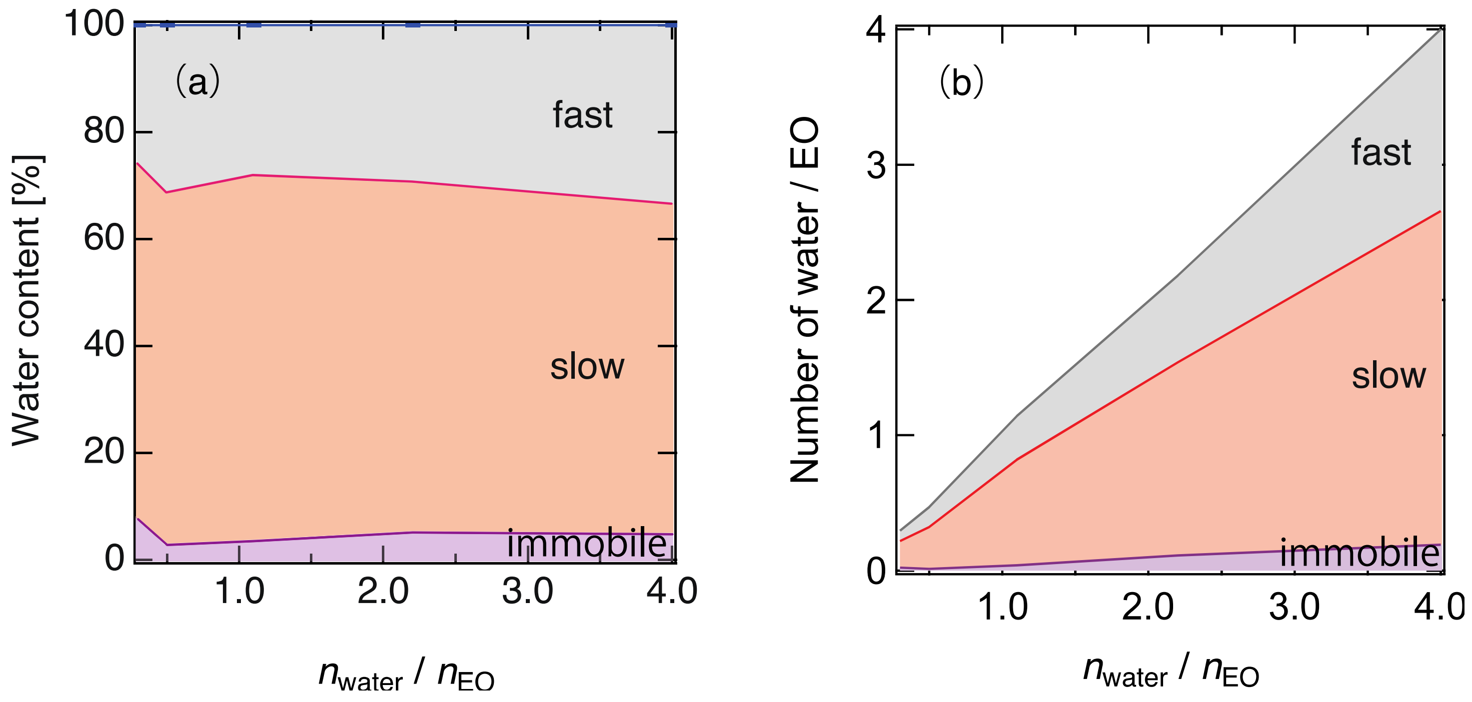
$$\Gamma = \frac{DQ^2}{1 + DQ^2\tau_0}$$

Diffusion coefficient

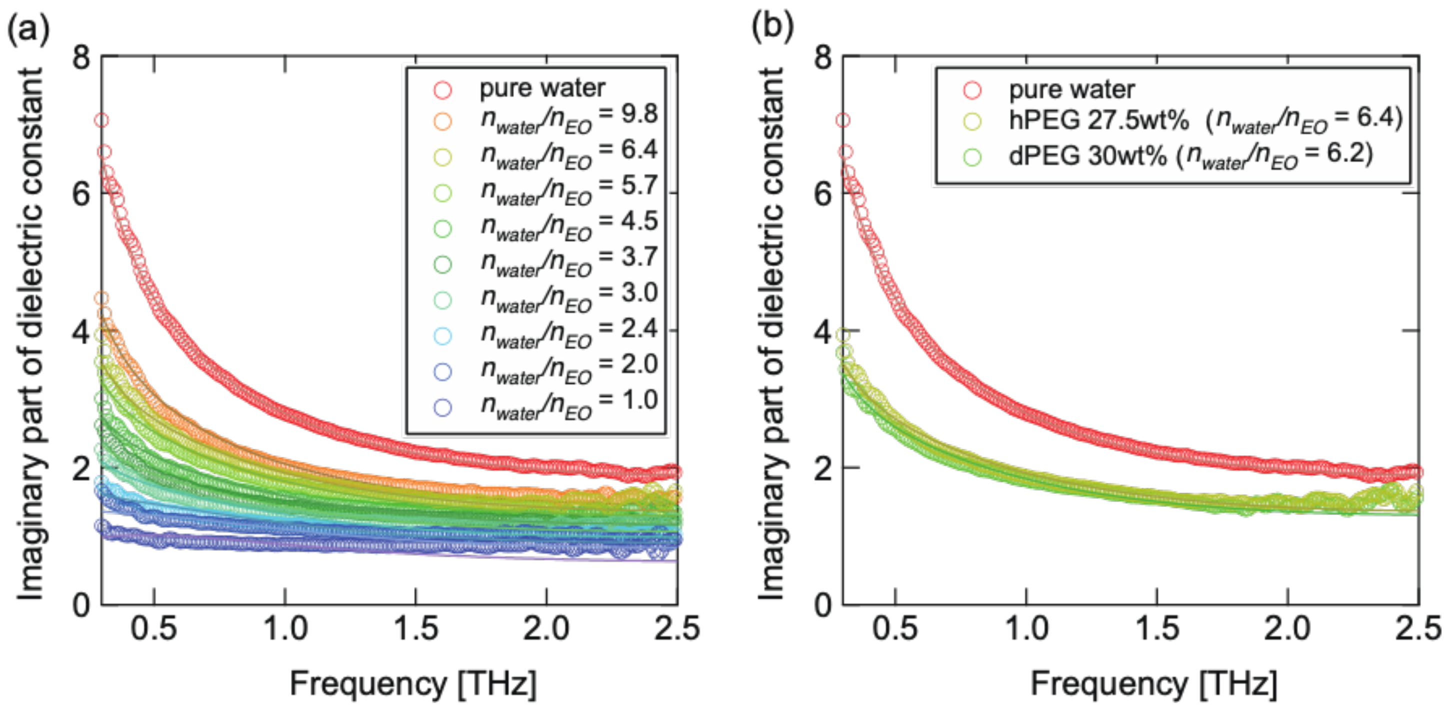


Diffusion coefficients of middle speed water, fast water, and PEO chains.

Fraction of water estimated by QENS

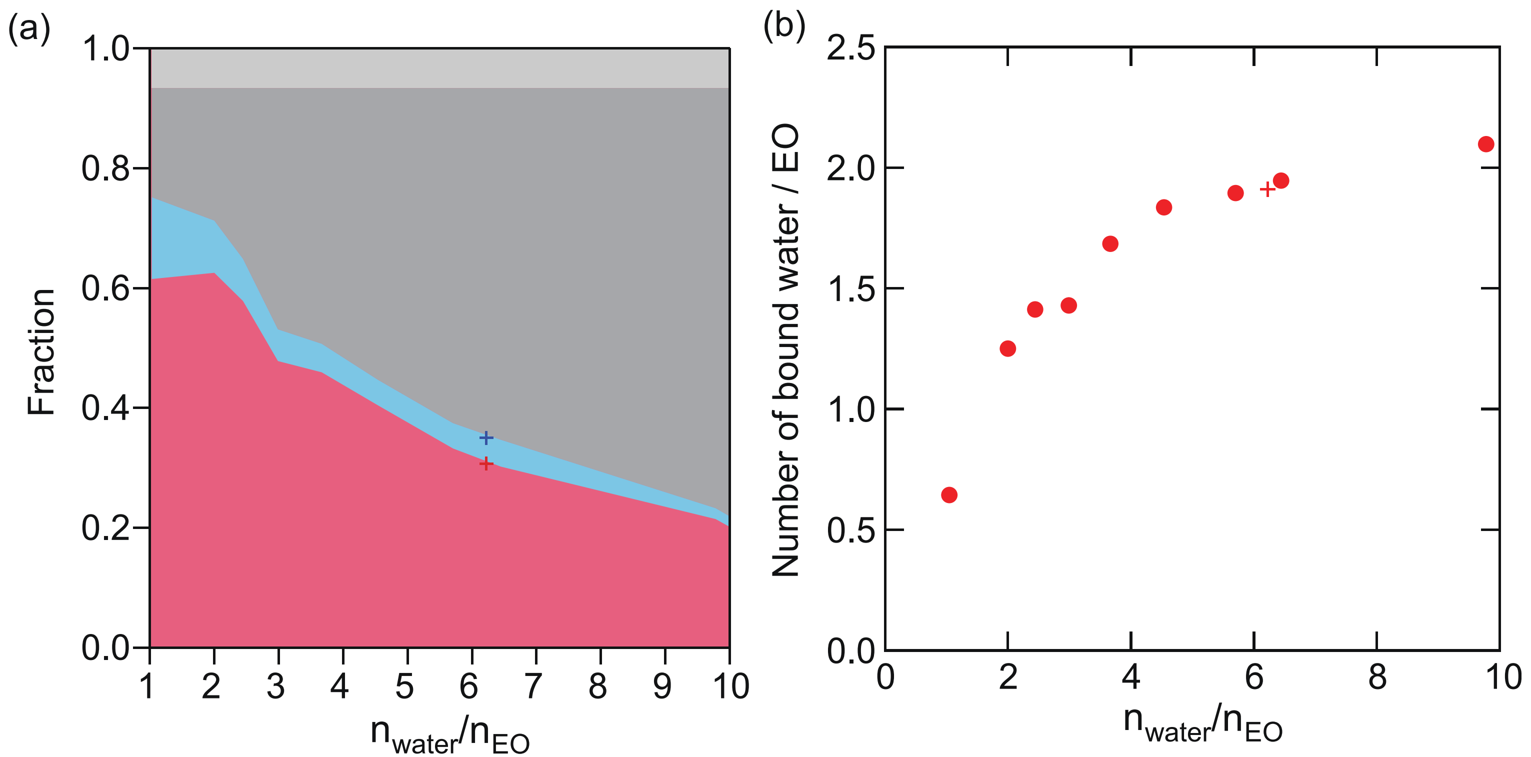


THz-TDR measurements



Imaginary part of the dielectric constant of PEO/H_2O solutions measured by THz-TDS. (a) Concentration dependences of *h*PEO/H_2O systems. (b) Comparison of *h*PEO/H_2O (n_{water}/n_{EO} = 6.4) and *d*PEO/H_2O (n_{water}/n_{EO} = 6.2). Solid lines indicate the fitting results.

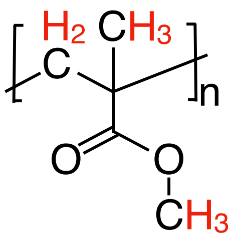
Water fraction estimated by THz-TDS



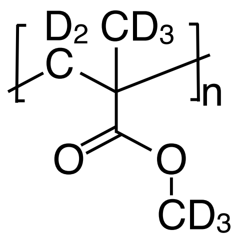
(a) n_{water}/n_{EO} dependence of each fraction of water estimated from THz-TDS in *h*PEO/H_2O solutions. Red: Bound water, Blue: Solute-induced isolated water, Gray: Free water (Light gray is isolated water that exists originally). Red and blue crosses indicate the results of *d*PEO/H_2O solution. (b) The number of bound water per monomer (EO) estimated from THz-TDS for (circles) *h*PEO/H_2O solutions, and (cross) *d*PEO/H_2O solution.

QENS experiments on PMMA/water

poly(methyl methacrylate) (PMMA): ポリメタクリル酸メチル（含水量2-3 vol%)



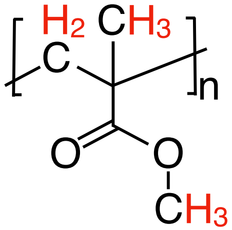
hPMMA: M_n=15k, M_w/M_n = 1.12

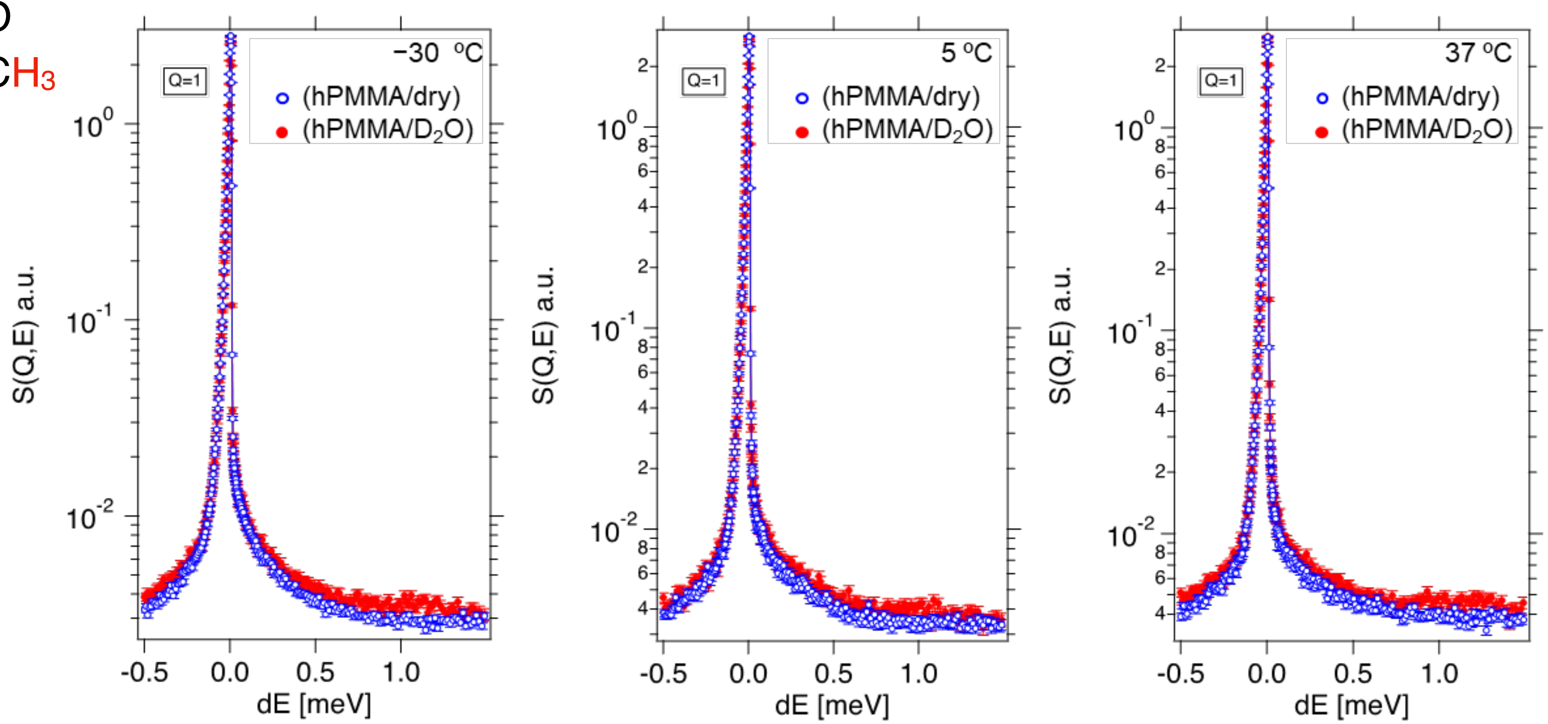


dPMMA: M_n=15.5k, M_w/M_n = 1.02

Y. Fujii, HS et al., Front. Chem., 2021

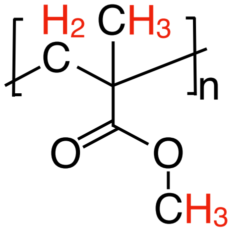
Effect of water on PMMA motion



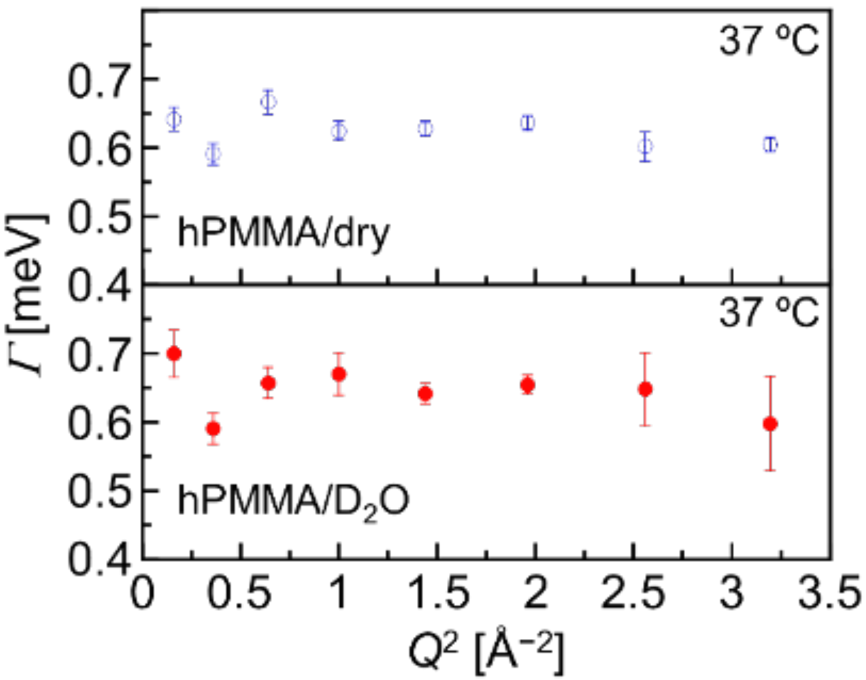


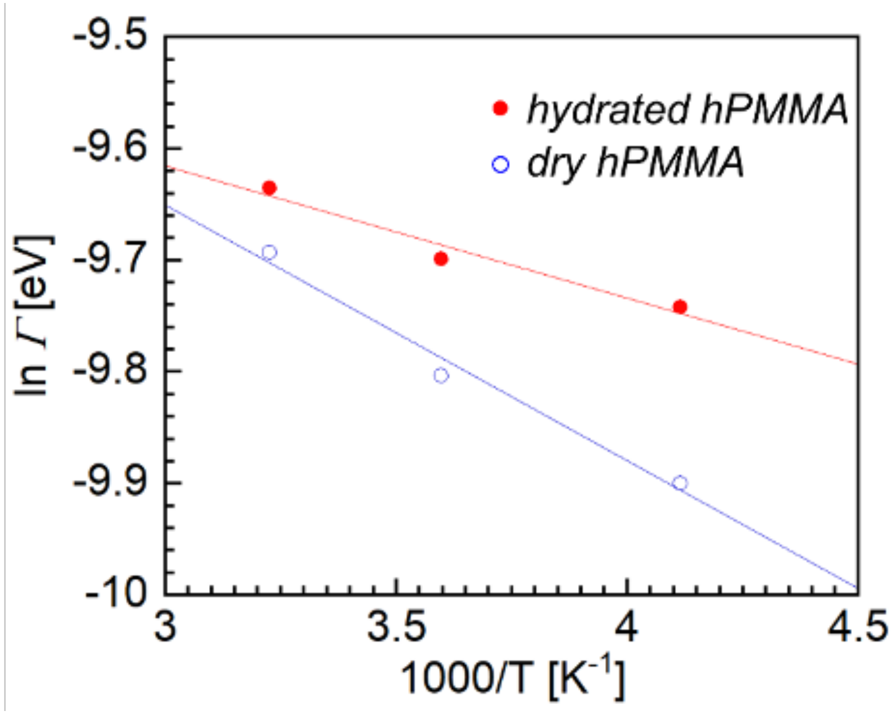
$$S(Q,E) = R(Q,E) \otimes (\nu_1 \delta(Q,E) + \nu_2 L(\Gamma, E)) + B_g,$$

Q- and T dependence of HWHM



$$\Gamma = \Gamma_{\infty}\exp(-\Delta H^{*}/k_{B}\cdot T)$$

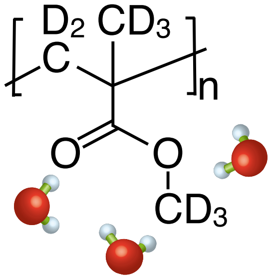


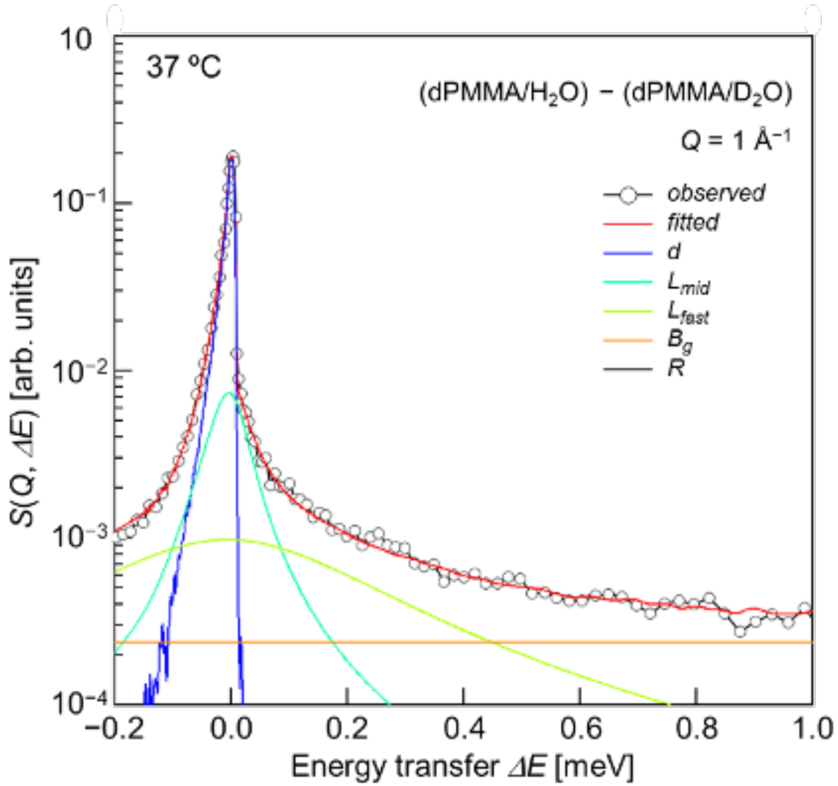


Q-independent: local motion

dry hPMMA: ΔH* = 5.1 kJ/mol
hydrated hPMMA: ΔH* = 5.1 kJ/mol

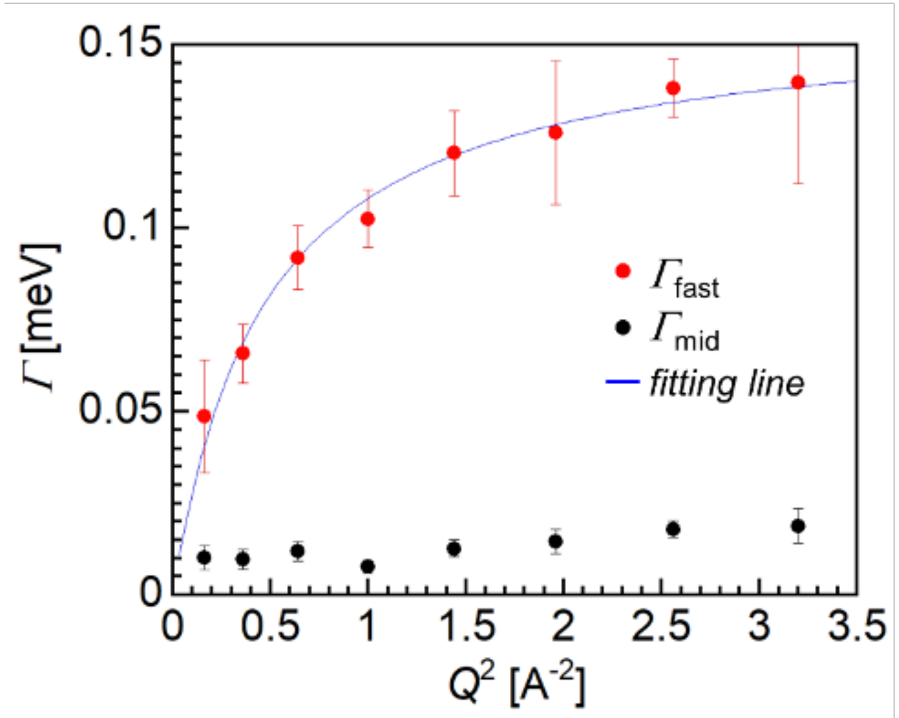
Hydration water dynamics





$$S(Q,E) = R(Q,E) \otimes (\nu_1 \delta(Q,E) + \nu_2 L_{\mathrm{mid}}(\Gamma_{\mathrm{mid}}, E) + \nu_3 L_{\mathrm{fast}}(\Gamma_{\mathrm{fast}}, E)) + B_g$$

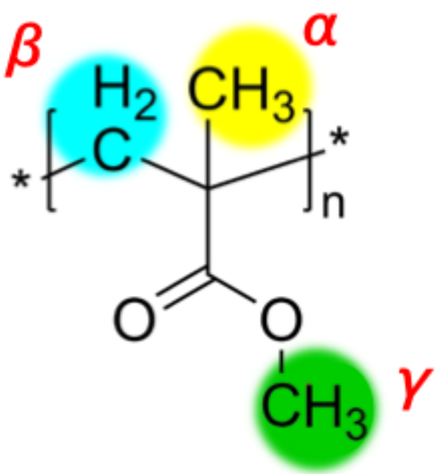
Q^2-dependence of HWHM



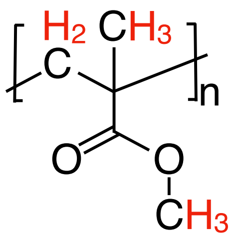
$$\Gamma = Dq^2/(1+Dq^2\tau)$$

D_{fast} = 1.3 x 10^{-9} m^2/s : about a half of the value for bulk water
τ_{fast} = 2 x 10^{-11} s: more than 3 times smaller than that of bulk water

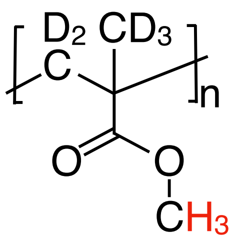
Partial deuteration of PMMA



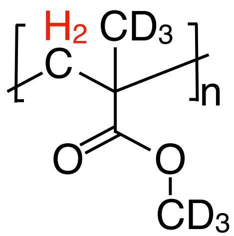
① $= \alpha + \beta + \gamma$
② $= \gamma$
③ $= \beta$
① $-$ ② $= \alpha + \beta$
① $-$ ③ $= \alpha + \gamma$
① $-$ ② $-$ ③ $= \alpha$



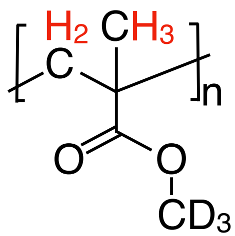
h8-PMMA



d5-PMMA



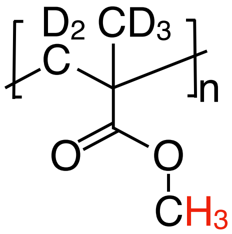
d6-PMMA



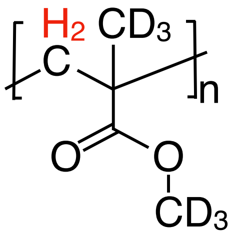
d3'-PMMA

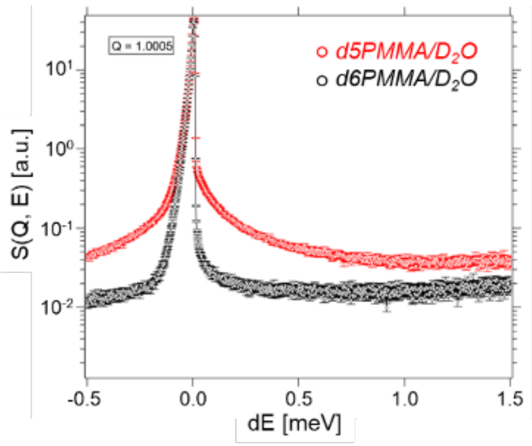
Q-E map

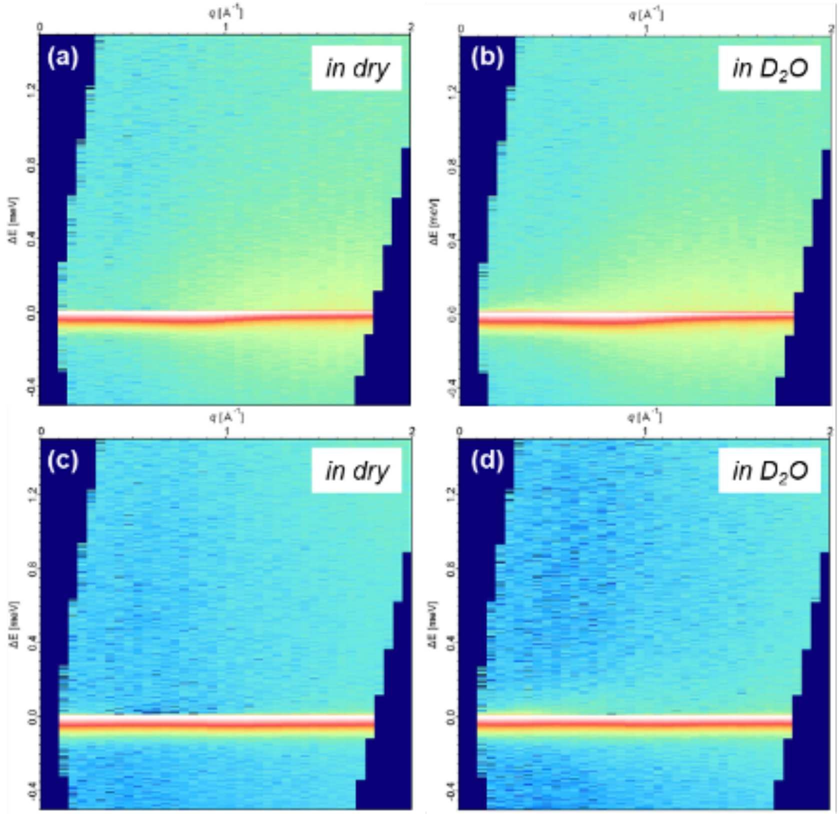
d5-PMMA



d6-PMMA

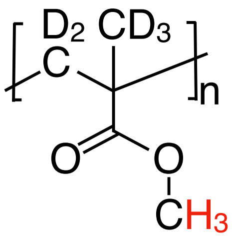


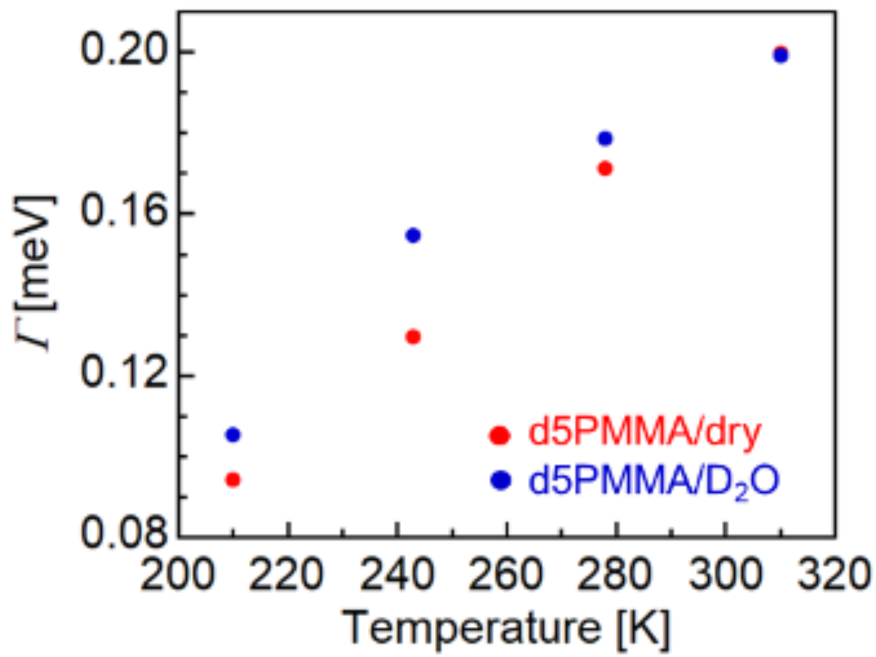


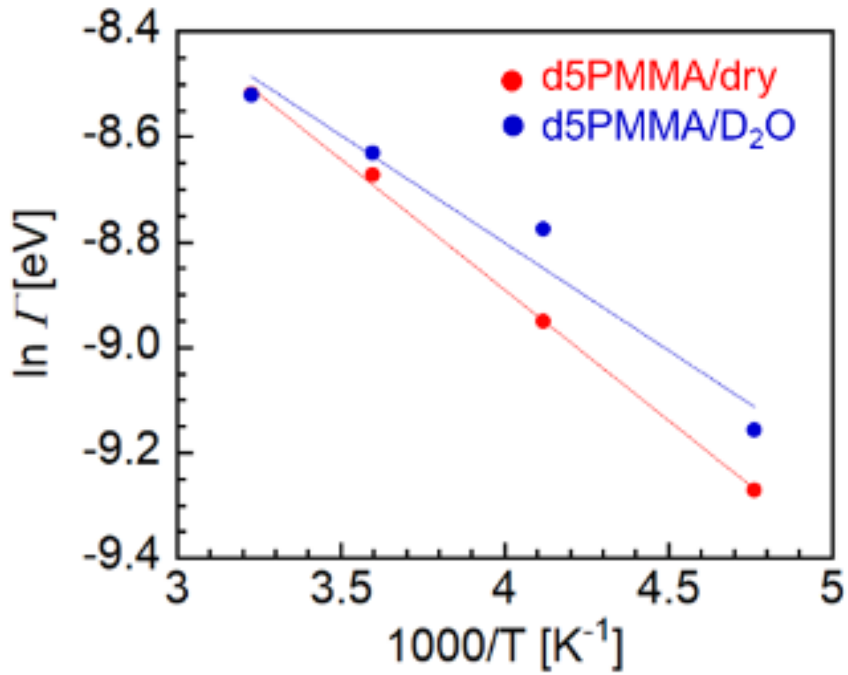


Effect of water

d5-PMMA







Summary

- QENS is a powerful method to investigate dynamic behaviors of biocompatible material and hydration water.
- We have investigated the dynamics of hydration water in the vicinity of lipid membranes, PEO and PMMA. These results indicate that the dynamics of hydration water is affected by the interaction with biocompatible materials.
- Further experiments on other biocompatible polymers will be (have been) performed and the origin of the biocompatibility will be clarified.