Water Dynamics in Confinement: Insights from NMR experiments

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Outline

• Introduction
• Basics of $^2$H NMR Experiments
• Water dynamics in protein matrices
• Water dynamics in silica matrices
• Summary
Bulk Water

Water anomalies:
Controversial discussion about the origin

Stanley et al.:
• Liquid-liquid phase transition (HDL-LDL)
• Existence of a second critical point

Nature (98), PNAS (05)

Structure
Changes in the order of the HB network

Paschek et al., CPC 08

Dynamics
Fragile-strong transition

Angell Science (08)
Confined Water

QENS

Hydrated lysozyme (h=0.3 g/g)

\[ E_a = 0.14 \text{ eV} \]

Chen et al., PNAS (06)

NMR diffusometry

Hydrated lysozyme (h=0.3 g/g)

Mallamace et al., JCP (07)

Evidence for a fragile-strong transition
**Confined Water**

### QENS

**Hydrated C-phycocyanin** (h=0.3)

**Hydrated myoglobin** (h=0.35)

![QENS Graph]

Doster et al., PRL 10

### Conductivity

**Hydrated lysozyme** (h=0.4)

![Conductivity Graph]

Chen

Pawlus et al., PRL (08)

No evidence for a fragile-strong transition
Confined Water

Dielectric spectroscopy

Crossover in the temperature dependence at \( T \approx T_g \)
Universal hydration water dynamics at \( T > T_g \) and at \( T < T_g \)

Cerveny et al., PRE (08)

\( E_a = 0.54 \) eV
Confined Water

\[ \log_{10}(\tau) \]

\[ \frac{1}{T} \]

\[ \alpha \]

\[ \beta \]

Chen et al., PNAS (05)
Liu et al., PRL (05)
Kumar et al., PRL (06)
Mallamace et al., JCP (07)

\[ T_g \]

\[ \alpha_{\text{conf}} \]

Cerveny et al., PRB (08)

\[ T_g \]

\[ \text{JG \beta} \]

Capaccioli et al., JPC B (07)
Ngai et al, JPC B (08)
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Basics of $^2\text{H}$ NMR Experiments

Quadrupolar Interaction

$^2\text{H}$: nuclear spin $I=1$

quadrupole moment $Q$

$H_Q = \frac{eQ}{2I(2I-1)\hbar} IVI$

$V_{\alpha\beta} = \frac{\partial^2 \Phi}{\partial r_{\alpha} \partial r_{\beta}}$

$\Phi$: electric potential

$\omega(\theta,\phi) = \pm \delta/2 \left[ 3\cos^2\theta - 1 - \eta \sin^2\theta \cos(2\phi) \right]$

$(\theta,\phi)$: polar coordinates of $\mathbf{B}_0$ in PAS of EFG tensors

$\delta$: anisotropy parameter, $\eta$: asymmetry parameter
Basics of $^2$H NMR Experiments

Quadrupolar Interaction for $\text{D}_2\text{O}$
($\eta \approx 0$)

The resonance frequency $\omega$ depends on the orientation of the O-D bond:

$$\omega(\theta) = \pm \frac{\delta}{2} (3\cos^2 \theta - 1)$$

Molecular reorientation renders $\omega$ time dependent.
Basics of $^2$H NMR Experiments

**Spin-lattice relaxation**

\[ \frac{1}{T_1} = C \cdot [J(\omega_L) + 4J(2\omega_L)] \]

\[ J(\omega) = \int_0^\infty F_2(t) \cos(\omega t) dt \]

$T_1$ minimum at $\omega_L \tau = 0.6 \rightarrow \tau \approx 10^{-9}$ s

**Line-shape analysis**

\[ \omega(\theta) = \pm \delta/2 (3\cos^2\theta - 1) \]

Motional narrowing at $\delta \tau = 0.6 \rightarrow \tau \approx 10^{-6}$ s

**Stimulated-echo experiments**

\[ F_2(t_m) = \langle \omega(0) \cdot \omega(t_m) \rangle \]

\[ 1/\delta \leq \tau \leq T_1 \rightarrow \tau \approx 10^{-3}$ s \]
2H NMR Spin-Lattice Relaxation

\[
\frac{1}{T_1} = \frac{2}{15} \delta^2 [J_2(\omega_0) + 4J_2(2\omega_0)] \quad J_2(\omega) = \int_0^\infty F_2(t) \cos(\omega t) dt
\]

Exponential correlation function (BPP)

\[ F_2(t) = e^{-\frac{t}{\tau}} \quad J_{BPP}(\omega) = \frac{\tau}{1 + \omega^2 \tau^2} \]

Distribution of correlation times \( G(\log \tau) \)

Cole-Davidson spectral density

\[ J_{CD}(\omega) = \omega^{-1} \sin[\beta_{CD} \arctan(\omega \tau_{CD})](1 + \omega^2 \tau_{CD})^{(\beta_{CD}/2)} \]

Cole-Cole spectral density

\[ J_{CC}(\omega) = \frac{\omega^{-1} \sin(\beta_{CC} \pi)(\omega \tau_{CC})^{\beta_{CC}}}{1 + (\omega \tau_{CC})^{2\beta_{CC}} + 2 \cos(\beta_{CC} \pi)(\omega \tau_{CC})^{\beta_{CC}}} \]
**2H NMR Line-Shape Analysis**

**Limit of slow motion:** \( \tau >> 1/\delta \approx 1\mu s \) (\( \eta = 0 \))

In crystalline powders and amorphous materials, a distribution of molecular orientations exists (powder average)

Due to the dependence of the frequency on the orientation, broad powder spectra are observed

\[
\omega(\theta) = \pm \frac{\delta}{2} (3\cos^2\theta - 1)
\]

\( \theta = 0^\circ \)

\( \theta = 90^\circ \)

M.H. Levitt

Spin Dynamics
**2H NMR Line-Shape Analysis**

**Limit of fast motion:** $\tau << 1/\delta \approx 1\mu s$ ($\eta=0$)

- **Isotropic Reorientation:** $\bar{\delta} = 0$, $\bar{\eta} = 0$
- **Uniaxial Reorientation:** $\bar{\delta} = \frac{\delta}{2}(3\cos^2\Psi - 1)$, $\bar{\eta} = 0$

**Isotropic**

- $\tau << 1/\delta$
- $\tau >> 1/\delta$

**Uniaxial**

- $\tau << 1/\delta$
- $\tau >> 1/\delta$

**High temperature**

**Low temperature**
If a broad distribution of correlation times $G(\log \tau)$ exists, e.g., because of a broad distribution of activation energies $g(E_a)$.

Weighted superposition of a broad line and a narrow line (two-phase spectra)

$g(E_a)$ can be determined from the weight of the narrow line:

$$g(E_a) = \frac{dW(T)}{dT}$$
2D $^2\text{H}$ NMR Experiments

Evolution ($t_1$) and detection ($t_2$) times are limited by $T_2$

Mixing time $t_m$ is limited by $T_1 \gg T_2$
2D $^2$H NMR Experiments

Stimulated-echo sequence: $t_m$: mixing time

$t_1$, $t_2 < t_m \approx \tau < T_1$

$t_m \approx 10^{-5}-10^0$ s

Measure and correlate the frequencies at two times:

$$F_2^{SS}(t_m; t_p) = \langle \sin(\omega_1 t_1) \cdot \sin(\omega_2 t_2) \rangle$$

$$F_2^{CC}(t_m; t_p) = \langle \cos(\omega_1 t_1) \cdot \cos(\omega_2 t_2) \rangle$$

Analysis in frequency domain:

Vary $t_1$ and $t_2$ for constant $t_m$

2D NMR spectrum $S(\omega_1, \omega_2)$ results from 2D Fourier transformation

Analysis in time domain:

Vary $t_m$ for constant $t_1 = t_2 = t_p$

Rotational correlation function is obtained from analysis of echo height

$$F_2(t_m; t_p) = \langle \cos[(\omega_2 - \omega_1)t_p] \rangle$$
2D $^2$H NMR Spectra

**No reorientation**

$(\omega_1 = \omega_2)$

**Isotropic reorientation**

$(\omega_1 \neq \omega_2)$

S$(\omega_1, \omega_2)$ measures the joint probability of finding a frequency $\omega_1$ before the mixing time $t_m$ and frequency $\omega_2$ after this period.

**Defined jump-angle $\beta$**

Schmidt-Rohr and Spiess
Multidimensional NMR and Polymers
2H NMR Stimulated-Echo Experiments

Meaning of the evolution time

\[ F_2(t_m; t_p) = \langle \cos[(\omega_2 - \omega_1)t_p] \rangle \]

Variation of the evolution time enables adjustment of angular resolution of stimulated-echo experiments

short \( t_p \): poor resolution
(large angles)

long \( t_p \): high resolution
(small angles)
Meaning of the evolution time

Structural relaxation of supercooled liquids

Determination of jump angle $\phi$:

$$\frac{\tau(t_p \to \infty)}{\tau(t_p \to 0)} = \frac{3}{2} \sin^2 \phi$$


Evolution-time dependence $\tau(t_p)$ provides access to jump angles
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**Biological Background**

Interactions between protein and water are essential for biological functions.

**Bacteriorhodopsin**

Temperature-dependent experiments yield valuable insights.

Fenimore et al., PNAS (2002)

Hydrated proteins:

Dynamical transition at 200-220 K is often accompanied by an onset of the biological function.
Biological Background

Connective Tissue
- amorphous ground substance
- collagen fibers (tensile strength)

elastin fibers (elasticity)

Skeletal Muscle

myoglobin
warrants oxygen transport
**Samples**

Elastin + D$_2$O  
Collagen + D$_2$O  
Myoglobin + D$_2$O

$^2$H NMR studies on the dynamical behaviors of protein-water mixtures

Low hydration levels $h = 0.2$-1.0 (g water/ g protein)
Due to proton exchange, a fraction of deuterons arrives at proteins

**Collagen + D$_2$O**

M. V.,
PRL 101, 225701 (08)

Magnetization builds up in two steps:

1. step ($T_{1W}$): supercooled water
2. step ($T_{1P}$): protein

Signal from protein hydration waters can be singled out in partially relaxed experiments.
**2H NMR Spin-Lattice Relaxation**

### Elastin/Collagen + D₂O

![Graph showing relaxation times for Elastin/Collagen + D₂O](image)

\[ \omega_L = 2\pi \cdot 76.8 \text{ MHz} \]

\[ \frac{1}{T_1} = C \cdot [J(\omega_L) + 4J(2\omega_L)] \]

\[ J(\omega) = \int_0^\infty F_2(t) \cos(\omega t) dt \]

BPP:

\[ F_2(t) = e^{-t/\tau} \]

\[ J_{BPP}(\omega) = \frac{\tau}{1 + \omega^2 \tau^2} \]

### Myoglobin + D₂O

![Graph showing relaxation times for Myoglobin + D₂O](image)

\[ \omega_L = 2\pi \cdot 46.1 \text{ MHz} \]

### Highly comparable water dynamics

Very broad distribution \( G(\log \tau) \)
$^{2}$H NMR Spin-Lattice Relaxation

**Elastin + D$_2$O**

![Graph showing $T_1$ relaxation data for Elastin + D$_2$O.]

$h = 0.43$

**Myoglobin + D$_2$O**

![Graph showing $T_1$ relaxation data for Myoglobin + D$_2$O.]

$h = 0.35$

**DS:** Gainaru et al.

$$g(E) \propto \exp\left(\frac{E - E_a}{2\sigma^2}\right) \quad E_a = 6330K \quad \sigma = 580K$$

**DS:** Jansson & Swenson

$$\varepsilon_{CC} = \varepsilon_\infty + \frac{\Delta \varepsilon}{1 + (i\omega \tau_{CC})^{\alpha_{CC}}}$$

Cole-Cole

$\alpha_{CC} = 0.48$

NMR and DS yield nicely consistent results
No indication of a fragile-strong transition at ca. 225 K
Gaussian distribution of activation energies $g(E_a)$
**2H NMR Line-Shape Analysis**

Myoglobin + D$_2$O

- **T ≥ 210K:**
  - Fast isotropic reorientation
  - ($\tau < 1/\delta \approx 1\mu$s)

- **210K ≥ T ≥ 140K:**
  - Fast anisotropic reorientation
  - ($\tau < 1/\delta \approx 1\mu$s)

- **140K > T:**
  - Absence of reorientation on a time scale of $1/\delta \approx 1\mu$s

Mechanism for water dynamics changes at ~ 210-220 K

Lusceac et al. (BBA 10)
Crossover from isotropic to anisotropic rotational motion on the microsecond time scale upon cooling through T\(\approx\)210-220 K

\(\tau<1/\delta\) and \(\tau>1/\delta\)

Lusceac et al. (JPC B 10)
Mechanisms for Low-Temperature Motion

Myoglobin + D₂O (h=0.35)

191K

π flip

\[ \chi = 101.4^\circ \]

3-site jump

\[ \chi = 130^\circ \]

distorted tetrahedral jump

\[ 85^\circ \]

Anisotropic large-angle (90-130°) jumps with a distribution of geometries?
Below 200 K, water shows anisotropic reorientation, which has a large amplitude, but no well-defined geometry.
Low-temperature water reorientation is characterized by:

Non-exponentiality

Large-angle jumps


M.V.
PRL (2008)
**1H NMR Diffusometry**

Application of a magnetic field with a field gradient $\mathbf{g}=(0,0,g)$:

$$\omega(z) = -\gamma(B_0 + g z)$$

**Investigation of translational diffusion**

**Static field gradients (SFG)**

- $\omega_1(z)$
- $\omega_2(z)$
- $t_p \leq T_2$
- $t_m \leq T_1$

higher gradients, more stable

**Pulsed field gradients (PFG)**

- $\omega_1(z)$
- $\omega_2(z)$
- $t_p \leq T_2$
- $t_m \leq T_1$

higher SNR, spectral resolution

For normal diffusion: $S = S_0 \exp\left(-q^2 D t_m\right)$

$q = g \gamma t_p$ bzw. $q = g \gamma \delta$

$D = 10^{-15} - 10^{-9} \text{ m}^2/\text{s}$

$1/q \approx 100 \text{ nm}$
**Myoglobin + H$_2$O: high temperatures**

Hydration water shows long-range translational diffusion

\[ S = S_0 \exp\left(-q^2 D t_m\right) \]

\[ q = g \gamma t_p \]

Rosenstihl et al. (JCP 11)
At low temperatures, stimulated-echo amplitude does not decay due to water diffusion, but rather due to cross relaxation.
**1H SFG NMR Diffusometry**

**Temperature-dependent diffusion coefficients**

![Graph showing temperature-dependent diffusion coefficients](image)

- Kink in temperature dependence due to onset of cross relaxation

**Translational motion vs. rotational motion**

![Graph showing translational motion and rotational motion](image)

- Different temperature dependence of rotational and translational motion

\[ D_c = f \frac{\Gamma a^2}{6} \]

MD simulation:
- \( f = 0.4 \)
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**Samples**

**D$_2$O (80% & 90%) in MCM-41 (C14)**

Pore diameter: 2.9 nm

Yoshida et al., JCP (2008)
Buildup of magnetization occurs in
- 1 step at high temperatures
- 3 steps at low temperatures

In the following: suppression of ice signal
2H NMR Spin-Lattice Relaxation

Dynamically distinguishable water species
Kink in the temperature dependence at T~210 K
Fast relaxation step vanishes upon cooling
$^2$H NMR Spin-Lattice Relaxation

**Correlation times**

Cole-Cole spectral density (symbols)

$\beta_{CC} = 0.59$ (80%)

$\beta_{CC} = 0.40$ (90%)

Cole-Davidson spectral density (crosses)

$\beta_{CD} = 0.30$ (80%)

$\beta_{CD} = 0.18$ (90%)

Kink in temperature dependence at 210 K ???

Distribution of correlation times $G(\log \tau)$
A fraction of water molecules shows liquid-like dynamics down to $T \sim 200$ K

Dynamically distinguishable water molecules: continuous and/or bimodal distribution $G(\log \tau)$?
$^2\text{H NMR Stimulated-Echo Decays}$

**Correlation functions**

$F_{2}^{CC}(t_m, t_p) = \langle \cos(\omega_1 t_p) \rangle \cos(\omega_2 t_p)$

*Non-exponential correlation function*

*Finite plateau at intermediate times*

**Temperature dependence**

$F_{2}^{CC}(t_m) = (1-F_\infty) \cdot \exp \left[ -\left( \frac{t_m}{\tau_K} \right)^\beta \right] + F_\infty$

*Diverse temperature dependence from spin-lattice relaxation and stimulated-echo experiments*

$E_a = 0.54 \text{ eV}$
Comparison of Correlation Times

Temperature dependence:
Consistent with neutron scattering data at high temperatures
Consistent with dielectric spectroscopy data at low temperatures
$^2$H NMR Stimulated-Echo Decays

Evolution-time dependence

Plateau height decreases with increasing angular resolution

$$F_2^{cc}(t_m; t_p) = \langle \cos(\omega_1 t_p) \cdot \cos(\omega_2 t_p) \rangle$$

$$F_2^{cc}(t_m) = (1 - F_\infty) \cdot \exp \left[ -\left( \frac{t_m}{\tau_K} \right)^\beta \right] + F_\infty$$
**2H NMR Stimulated-Echo Decays**

**Evolution-time dependence**

**Correlation times**

- Large angle jumps
- Water
- Small angle jumps (glycerol, Böhmer et al.)

**Plateau height**

- Distorted \(\pi\)-flip + tetrahedral jump

**Graphs:**

1. **Correlation times:**
   - \(\tau(t_p) / \tau(t_p = 0)\) versus evolution time \(t_p\) in µs.
   - Data points for different samples.
2. **Plateau height:**
   - \(F(8)\) versus evolution time \(t_p\) in µs.
   - Graphs for different types of motion.

**Legend:**

- Four site jump
- Fully isotropic jump
- Random jump on a cone
- Superposition of motions
- Liquid at temperature \(T = 191.3\) K

**Large-angle jumps**

**Distorted anisotropic motion**
Summary

**Water in protein matrices**
shows no fragile-strong transition but a crossover from isotropic to anisotropic reorientation

The change of mechanism for rotational motion may be related to a crossover from diffusive motion to localized motion

**Water in silica matrices**
exhibits distinguishable dynamical processes

The processes dominating above and below ~210K, respectively, have different temperature dependence

**All surface waters**
show universal low-temperature dynamics which involves large-angle jumps with distributions of motional geometries and correlation times
Thank You

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**13C CPMAS NMR Spectra**

**Hydrated Elastin (h=0.6 g/g)**

**13C MAS NMR**

**Elastin dynamics:**
- requires an existence of a hydration shell
- freezes in upon cooling through 200-230 K

Lusceac et al., BBA (2010)

Perry et al., BJ (2002)