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Double-quantum NMR methods: investigating (supra) molecular structure

- Internuclear proximities, chemical shifts and π-shifts
- Measurement of internuclear distances

$^1$H-$^1$H homonuclear

$^1$H-$^1$3C/$^15$N heteronuclear
**NMR methods: investigating molecular dynamics**

**Fast local dynamics**
- **Rigid**
- **Mobile**

**Slow reorientations**
- **Jump sites**
- **Jump angle**

**Averaging of dipolar couplings**

**Loss of NMR signal**

**Exchange NMR experiments**

<table>
<thead>
<tr>
<th>Fast</th>
<th>Intermediate</th>
<th>Slow</th>
<th>Static</th>
</tr>
</thead>
<tbody>
<tr>
<td>(10^{-7})</td>
<td>(10^{-6})</td>
<td>(10^{-5})</td>
<td>(10^{-4})</td>
</tr>
</tbody>
</table>

**Motional correlation time [seconds]**
Merging solid-state and solution-state NMR methods

**Solution State**
- Pulsed Field Gradients
- Inverse Detection (\(^1\)H)

**Solid State**
- Fast Magic-Angle Spinning
- Dipolar Decoupling and Recoupling

**Goals**
- **Resolution Enhancement**
- **Sensitivity Enhancement**
- Measuring Molecular Structure and Conformation/Packing

**Techniques**
- Solids and Materials at the Solid/Liquid Borderline

**1H**
- natural abundance
- \(^{15}\)N in L-histidine
Outline of the Talk

- Homonuclear DQ NMR spectroscopy under fast MAS
- Residual dipolar couplings and order parameters in nematic LC
- Multi-Spin Effects in abundant spin systems
  - two spin approximation and its limits
  - double-quantum relay in dipolar systems
  - multi-spin coherences involving more than 2 spins
- Conclusions for homonuclear DQ NMR in dense spin systems

- Heteronuclear MQ NMR spectroscopy and REDOR
- Shape persistent polymers with dendritic sidegroups
- Inverse detection of $^{15}$N in natural abundance
- Conclusions
## High Resolution Double-Quantum NMR in Solids

Properties of double-quantum coherences:

\[ \omega_{DQ} = \sum_i \omega_{SQ,i} \]

\[ I_{DQ,ij} = f(D_{ij} \cdot t) \]

\[ \frac{dM}{dt} \approx 0 \]

High resolution solid-state NMR spectroscopy: average out dipolar coupling via

- Multi pulse sequence (WAHUHA, MREV-8)
- Magic Angle Spining (MAS)

Problem: Coupling between the spins is needed for double-quantum excitation!

<table>
<thead>
<tr>
<th>excitation</th>
<th>evolution ( t_1 )</th>
<th>reconversion</th>
<th>detection ( t_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \omega_R \approx 0 )</td>
<td>( \omega_R &gt; D_{ij} )</td>
<td>( \omega_R \approx 0 )</td>
<td>( \omega_R &gt; D_{ij} )</td>
</tr>
</tbody>
</table>
**Dipolar Couplings and Sample Rotation at the Magic Angle**

**Dipole Dipole Coupling:**

\[
\hat{H} \propto \frac{1}{3} \cdot \frac{1}{2} (3 \cos^2 \theta_{ij} - 1) \gamma_i \gamma_j (2 \hat{I}_{z,i} \hat{I}_{z,j} + \hat{I}_{+,i} \hat{I}_{-,j} + \hat{I}_{-,i} \hat{I}_{+,j})
\]

**Magic Angle Spinning:**

- **Spatial part:** Unchanged
- **Spin part:** \( \rightarrow 0 \)
Excitation of Double-Quantum Coherences under MAS

Direct Excitation

\[ D_{ij} > \omega_R \]

\[ \tau < 0.5 \cdot \tau_R \]

no synchronization

3 Pulse Sequence
(+ z-filter)

Recoupling

\[ D_{ij} < \omega_R \]

\[ \tau = n \cdot \tau_R \]

rotor synchronization

- DRAMA
- BABA
- C7

In the regime of fast MAS only recoupling techniques are applicable.
Recoupling Pulse Sequences

Average Hamiltonian of Pulse Sequences:

\[ H^0_{av} = \sum_{i<j} \omega_{PF} I_i^+ I_j^+ + \omega_{PF}^* I_i^- I_j^- \]

Labourotory-System Pulse Sequences
examples: DRAMA, Back-to-Back, REDOR...

orientation dependence of DQ excitation efficiency

Rotor-System Pulse Sequences
examples: C_7, POST C_7, MELODRAMA ...

orientation dependence of DQ excitation efficiency
Double Quantum Spectroscopy under fast MAS

The rotor modulation of the recoupled dipolar Hamiltonian due to $t_1$-increments $\Delta t_1 \neq \tau_R$ leads to MAS sideband pattern in the $t_1$ dimension, which depend on the recoupling time and the dipolar coupling only.
Local Order in Nematic Liquid Crystals

Double-quantum measurements are in good agreement with $^2$H experiments.

Structure of a nematic liquid crystal

Chemical structure of nematic model compound.

DQ build-up behaviour
DQ sideband pattern

local order parameter

$S = \langle \frac{1}{2} (3 \cos^2 \theta - 1) \rangle = 0.6$
**Dipolar Coupling and Order Parameters**

DQ coherence

<table>
<thead>
<tr>
<th></th>
<th>A-C</th>
<th>B-C</th>
<th>D-D</th>
<th>E-E</th>
<th>F-F</th>
<th>G-G</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>D_{ij,eff.}</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>4.8</td>
<td>4.9</td>
<td>5.2</td>
<td>5.2</td>
<td>4.8</td>
<td>3.1</td>
</tr>
<tr>
<td>[kHz]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Build-up</td>
<td>4.4</td>
<td>4.3</td>
<td>4.5</td>
<td>5.6</td>
<td>4.3</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>S_{ij}</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>0.58</td>
<td>0.59</td>
<td>0.50</td>
<td>0.50</td>
<td>0.46</td>
<td>0.30</td>
</tr>
<tr>
<td>Build-up</td>
<td>0.52</td>
<td>0.53</td>
<td>0.42</td>
<td>0.54</td>
<td>0.40</td>
<td>0.22</td>
</tr>
</tbody>
</table>

**Graphs:**
- BC DQ coherence
- DQ-Preparation Time [ms]
- DQ Intensity [a. u.]
- Order parameter S
- DQ coherences
- DQ-Preparation Time [ms]
- DQ Intensity [a. u.]
- Order parameter S

**Diagrams:**
- BC DQ coherence
- DQ-Preparation Time [ms]
- DQ Intensity [a. u.]
- Order parameter S
Multi-Spin Effects in Double-Quantum Build-Up

2-spin approximation describes only the initial behavior.
Multi-spin effects lead to exponential decay of the DQ intensities.
Multi-Spin Effects in DQ Sideband Pattern

1st order sidebands are under estimated by 2-spin approximation
DQ Polarisation Transfer: 1. Order Relay

double-quantum experiment:

| excitation | $t_1$ | reconversion | $t_2$ |

1. Order DQ relay

$\text{t}_1$ evolution → reconversion → $t_2$ detection

Double-quantum polarisation transfer leads to negative signal intensities
**DQ Polarisation Transfer: 2. Order Relay**

**Double-quantum experiment:**

- **Excitation** $t_1$
- **Reconversion**
- **$t_2$**

**2. Order Double-quantum Relay**

- **$t_1$ Evolution**
- **Reconversion**
- **$t_2$ Detection**

For longer double-quantum recoupling times, coherences get delocalised and can obscure the double-quantum spectrum.
Dipolar couplings lead to more complicated relay behavior than J-coupling.
4 spin 2 quantum coherences

\[ H_{4S2Q} = a_{ijkl} I_i^+ I_j^+ I_k^- I_l^- + a_{ijkl}^* I_i^- I_j^- I_k^+ I_l^+ \]

\[ (I_A^+ I_C^- I_C^+ I_D^- + I_A^- I_C^+ I_C^- I_D^+) \text{ coherence} \]

Multi-spin DQ coherences can be observed, but are hard to analyse.
Conclusions for $^1$H DQ NMR Spectroscopy

- High resolution DQ spectra under fast MAS can be obtained using appropriate recoupling sequences.

- DQ build-up behavior and DQ spinning sideband pattern provide quantitative information about dipolar couplings.

- Even though, multi-spin effects are observed, a careful 2-spin analysis provides reasonable dipolar coupling values.

- In favorable cases, multi-spin effects can be analyzed and additional information can be obtained.

- DQ relay intensities due to dipolar couplings are harder to analyze than those due to J-couplings.
How dipolar interactions “explore” space

homonuclear case:
random walk characteristics, delocalized

heteronuclear case:
well-localized probing of the $^{13}$C environment

approaching incoherent diffusive processes
Rotational Echo Double Resonance (REDOR)

$I$ ($^1H$) \[ \text{CP} \rightarrow \text{DD} \rightarrow \text{DD} \]

$S$ ($^{13}C$) "detected"

$L$ ($^{15}N, ^{19}F, \ldots$) "passive"

rotor position

\[ S_Y \frac{1}{2N \tau_R} S_Y L_Z \rightarrow S_Y \cos(N\Phi) - 2S_X L_Z \sin(N\Phi) \rightarrow S_Y \left[ \cos^2(N\Phi) \pm \sin^2(N\Phi) \right] = \begin{cases} S_Y \\ S_Y \cos(2N\Phi) \end{cases} \]
**Internuclear distances from REDOR curves**

Experiments in Asparagine

<table>
<thead>
<tr>
<th>Table 1. Internuclear Distances in [U-13C,15N]Asparagine</th>
</tr>
</thead>
<tbody>
<tr>
<td>atoms&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>( N' )</td>
</tr>
<tr>
<td>C(^\alpha)</td>
</tr>
<tr>
<td>C(^\beta)</td>
</tr>
<tr>
<td>( N^{\delta 2} )</td>
</tr>
<tr>
<td>C(^\alpha)</td>
</tr>
<tr>
<td>C(^\beta)</td>
</tr>
</tbody>
</table>
Coherent polarisation transfer

REDOR scheme

Heteronuclear correlation (SQ-SQ) via transferred echo double resonance (TEDOR)

Heteronuclear single-quantum correlation (HSQC) via recoupled polarisation transfer (REPT)
From deuterons to $\text{CH}_n$ groups

Selectively placed **deuterons** as probes for molecular dynamics (quadrupole coupling of spin-1 nucleus)

Regular $\text{CH}_n$ groups

- use of dipole-dipole coupling between C and H
- no additional synthetic effort
  - no selective placement of probing nucleus
  - no isotopic enrichment
- assignment of dynamics by $^{13}\text{C}$ chemical shifts
- handling of CH, CH$_2$ and CH$_3$ groups
- interferences of multiple C-H couplings
- decoupling from surrounding $^1\text{H}$
Two alternative concepts for measuring recoupled interactions:
• following the signal intensity as a function of the recoupling time (resulting in build-up or dephasing curves)
• recording rotor-encoded signal (resulting in MAS sideband patterns)
Cylindrical self-assembly of dendritic sidegroups (I)

Materials:
V. Percec

**REREDOR**
- **OCH$_2$ group**
  - $\tau_{\text{exc}} = 4 \tau_R = 133\mu$s
  - $D_{\text{CH}} = 17.0$ kHz ($S = 81\%$)

- **OCH$_2$ group**
  - $\tau_{\text{exc}} = 4 \tau_R = 133\mu$s
  - $D_{\text{CH}} = 12.0$ kHz ($S = 57\%$)

- **aromatic CH group**
  - $\tau_{\text{exc}} = 4 \tau_R = 133\mu$s
  - $D_{\text{CH}} = 21.0$ kHz ($S \sim 100\%$)

**REPT-HDOR**
- **aromatic CH group**
  - $\tau_{\text{exc}} = 8 \tau_R = 320\mu$s
  - $D_{\text{CH}} = 6.0$ kHz ($S = 29\%$)
Cylindrical self-assembly of dendritic sidegroups (II)

- **dendritic sidegroup**
- **structure-directing moieties**
- **cylindrical assembly independent of molecule in the center (chain, discs)**
- **polymer chain**
- **stack of aromatic molecules**
Sensitivity enhancement by inverse ($^1$H) detection

33% $^{15}$N-enriched

0.35% $^{15}$N (natural abundance)

$S/N = 8$

$x\times10$

$S/N = 80$

$\delta_1$, $\delta_2$, $\varepsilon_1$, $\varepsilon_2$
Natural-abundance $^{15}\text{N}-^{1}\text{H}$ correlation NMR

preparation ($^{1}\text{H} \to ^{15}\text{N}$)  TEDOR/REPT experiment ($^{15}\text{N} \to ^{1}\text{H}$ transfer) with/without rotor-encoding

<table>
<thead>
<tr>
<th>CP</th>
<th>dephasing</th>
<th>$t_1$</th>
<th>recoupling</th>
<th>$t_1'$</th>
<th>recoupling</th>
<th>dephasing</th>
<th>detection</th>
</tr>
</thead>
</table>

$^{1}\text{H}$  $^{15}\text{N}$

RRR pulses  DD

rotor encoding

pulsed field gradients (PFGs)

$^{15}\text{N}$-$^{1}\text{H}$ chemical-shift correlation  $^{15}\text{N}$-$^{1}\text{H}$ dipolar couplings from rotor-encoded MAS sideband patterns
NH···O hydrogen bonds in L-histidine

2D chemical shift correlation:

δ₁-NH  ε₂-NH  NH₃⁺

2D chemical shift correlation
plus NH coupling information:

δ₁-NH  ε₂-NH  NH₃⁺

700 MHz ¹H frequency, 30 kHz MAS, ~ 15 mg sample.
N-H bond stretching due to hydrogen bonding

NH dipolar coupling from rotor-encoded spinning sideband pattern:

$\epsilon_2$-NH

$\delta_1$-NH

$\delta_1$-NH

20480 transients in total

$\omega/\omega_R$

$r_{NH} = (107 \pm 2) \text{ pm}$

$r_{NH} = (111 \pm 2) \text{ pm}$
Similarities of homo- and heteronuclear are sufficient to pursue the strategies known from $^1$H DQ NMR.

Rotor encoding can be used to measure heteronuclear dipolar couplings with REDOR based techniques.

The larger spread of chemical shifts of rare low $\gamma$ nuclei provides site selective information about molecular dynamics.

$^1$H detection of low $\gamma$ nuclei can increase the sensitivity and NMR measurements in natural abundance become feasible.
NMR on supramolecular systems

Homonuclear double-quantum measurements

✓ Dipolar couplings and order parameters in LC system  Michael Neidhöfer
✓ Analysis of $^1$H DQ relay                     Robert Graf

Heteronuclear method development in solid-state NMR

✓ $^{13}$C site-resolved dynamics of CH$_n$ groups  Kay Saalwächter
✓ natural abundance $^{15}$N-$^1$H correlation spectroscopy  Ingo Schnell
✓ N-H distance measurements

Investigations of complex systems

✓ Dynamics and self-assembly of dendritic sidegroups  Almut Rapp